# Henry Ford Hospital Medical Bulletin

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# CONTENTS


| | Page |
|---|---|
| 1. Medicine in India<br>JOHN K. ORMOND | 164 |
| 2. The Research Aspect of the Epileptiform Syndrone<br>LORNE D. PROCTOR, M.D.<br>ROBERT S. KNIGHTON, M.D. | 171 |
| 3. Newer Opium Antagonists, Their Actions and Use<br>PAUL R. DUMKE, M.D. | 176 |
| 4. The Hyponatremic Syndrome<br>ELLIOTT V. NEWMAN, M.D. | 180 |
| 5. Hormones of the Posterior Pituitary<br>VINCENT DU VIGNEAUD, Ph. D. | 187 |
| 6. The Diagnosis of Hepatic Pathology By Needle Biopsy<br>ROBERT J. PRIEST, M.D., WAYNE L. AGEY, M.D.,<br>HUGH H. STEELE, M.D. and JEROME W. FISCHBEIN, M.D. | 190 |
| 7. Dentistry for the Handicapped Child<br>WILLIAM F. VIA, JR., D.D.S., M.S. | 195 |
| 8. Description of New Orthopedic Appliances<br>"Matched" General Utility Retractors for Use in Orthopedic and Extremity Surgery.<br>An Adjustable Dual-Purpose "Overhead" Reading Table For Use on the Foster-Lyford Reversible Orthopedic Bed.<br>JOHN LYFORD, III, M. D. | 198 |
| 9. Friends of the Institute<br>OLIVER H. GAEBLER, Ph.D. | 202 |
| 10. Programs of Meetings | 204 |
| 11. Abstracts of Recent Publications of the Professional Staff of the Henry Ford Hospital and the Edsel B. Ford Institute for Medical Research | 208 |
| 12. Index | 214 |



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# HENRY FORD HOSPITAL MEDICAL BULLETIN

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# MEDICINE IN INDIA

JOHN K. ORMOND*

The disease picture of the people of India varies according to religion, latitude, altitude, rainfall, economic state, and literacy. A few facts will illustrate this: penile cancer is very common among Hindus but seldom seen in Moslems; "stomach" ulcer is frequent in the south and rare in the north while gall-bladder disease is common in the north and rarely seen in the south; mountain diarrhoea occurs in the hill country; malnutrition, leprosy, and tuberculosis are largely dependent on economic conditions.

The picture, in the last twenty years, is changing for the better. The change is due to the introduction of vaccines and antibiotics in addition to governmental campaigns for improved sanitation and against certain insects. Malaria is no longer universal. Plague is unknown, and cholera, while endemic, no longer comes in epidemic proportions. Typhoid has become rarer and typhus is not often seen. The tickborne diseases occur less frequently.

Roughly, the country can be divided into six regions: (1) the mountainous area of the north—the Himalaya region. (2) the great and fertile alluvial plain of the Ganges and the Indus which lies just south of these mountains. This region was the seat of old and resplendent empires, and the target of invasion from the north and west since the time of Alexander and before. (3) an old and partly leveled hill country running east and west across the upper part of the peninsula. This is the jungle area of Kipling's Mowgli stories. (4) the Deccan Plateau—a great area made of horizontal beds of lava, dissected into hills and plains. This plateau averages about two thousand feet above sea level. (5) the lower peninsula composed of old eroded Archaean mountains with their alluvial plains and valleys. (6) the coastal plain at or near sea level separated from the inland plateau by a range of hills—the Ghats. Of these divisions, the western and southern coastal plains and the plain of the Ganges are the most fertile and most thickly populated.

Through all these regions diversity of tongues is great. There is, however, a broad underlying unity of culture, modified somewhat by religion, climate, economic differences, and by the degree to which they have been exposed to the outside —especially to the western influences. Ninety percent, or nearly seven hundred thousand, of the people live in villages. The villages range in size from a few householders to communities of ten or twelve thousand inhabitants.

Everywhere, the bullock is the beast of burden, drawing the carts and ploughs, and hauling water from the wells for irrigation. Many little donkeys are seen. Horses are less common and usually small. In the north, camels are often seen ploughing, or walking the monotonous circle of the Persian pump, or drawing carts on the road.

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The water buffalo is the chief milk animal. However, milk goats are not uncommon, and in driving about the country, many herds of cows are met on the road. These animals are usually thin and poor, and for the most part with dry udders. Flocks of sheep and goats are everywhere. These animals are apparently grown more for their wool than for their flesh, for the Hindus are vegetarians. However, more and more eggs, fish and fowl are eaten when available. The Moslems eat meat when they can afford it. I was surprised to find some pigs scattered about the country, and I am informed that some of the outcastes and those of the lower caste eat pork.

Most of the villagers live in dismal, dark and insubstantial dwellings. In the south these are built of matting made from woven palm or reed. In the north sundried bricks or abdobe is used. The wealthy use stone when it is available or fired brick if it is not. Our city of Miraj is largely built of black basalt—a stone which underlies the whole area.

The native diet is protein-poor. In the north the staple is wheat, while in the far south it is rice and tapioca. In our region a maize-like grain is grown. Rice is grown and eaten everywhere. Sugar cane is seen in all parts of the country. Dahl, a legume, seems to be the chief source of protein. The food is usually highly seasoned and hot. Chili is freely used especially in the south. It is said that the farther south one goes the hotter the food, and this may have something to do with the prevalence of "stomach" ulcers in that part of the country.

The village water supply is usually from wells which are shallow and exposed to surface drainage. There is no sewage system. Animals (goats, dogs, cows and donkeys) wander at will. Traditionally, the place for defecation is the fields; however, to most villagers fields are not convenient, and adults use any vacant land. Children merely go outside the house. Our city which has a population of 40,000 has no sewage system. One open space, for obvious reasons, is known as the "Rose Garden." The sanitary problem is easily appreciated and is complicated by the level of education and the language situation.

There are eight *major* languages, but that number can be doubled if those of considerable importance are counted. There are over two hundred dialects. In general the languages of the north are derived from the Sanscrit, and those of the south are Dravidian in origin. This diversity of tongues makes intercommunication difficult. English, though known to only two percent of the people, is the only language spoken in all parts of the country. The government has decreed that Hindi, a Sanscrit language, is to be the national tongue. However, this is meeting with much opposition in the south. Over eighty-five percent of the people are illiterate.

Before the British era, some parts of the country had been subject to periodic unrelievable famines, to the unchecked ravages of cholera, plague, malaria and other diseases. The British either built or stimulated the building of irrigation systems. They built railroads and highways. At the present no part of the country is out of reach of relief from famine.

The British introduced scientific medicine. They founded or stimulated the founding of universities in the larger cities where science, engineering, medicine and law were taught in English. The English language became the language of government, of railways, of the post office, and in any other field where rapid and free intercommunication was desirable or necessary. This meant that a knowledge of English was a prerequisite to the study of medicine. It also opened the great store of English textbooks to the student and freed him from being confined to his own language district in obtaining his education.

Government hospitals were built, institutions for the care and treatment of those infected with tuberculosis and leprosy were established. A system of village dispensaries with regional or district medical and surgical officers was instituted. Since the departure of the British, the Indian government, national and state, has built more hospitals and expanded the program greatly. Some new medical schools with excellent equipment have been built; however, the need for primary education is so vast that funds for medical education are limited.

Christian missions are an important part of the medical picture. There are three Christian medical schools as well as numerous hospitals averaging twenty-five to one hundred and fifty beds. Many of these hospitals have training schools for nurses. The Christians also have many village dispensaries, some of which are managed by doctors and others by nurses. The dispensary may be connected with a mission hospital or medical school. It may be without formal association with any institution, yet have cordial relations with the nearby mission or government hospital. In general, I believe, the mission institutions penetrate a little deeper than those of the government into the mass of the population. The government schools are in the large cities, while the three mission schools are in the smaller cities of Vellore, Ludhiana and Miraj. Most of the hospitals are in the smaller cities and some in villages, like those at Kutchwa and Mungeli which are well known.

There are twenty medical schools and colleges in India. About one thousand students graduate from these schools each year. Obviously, in a country of three hundred and fifty million this number cannot meet the need. It is estimated that there is one doctor to about forty-five thousand people. The same is true of nurses. Most of the graduates of the larger schools settle in the cities where the demand for their services is great, the monetary rewards larger, and living conditions for them and their families more satisfactory. Until recently a few of the schools, such as Miraj, did not prepare graduates for the M. B. B. S. degree which corresponds to our M.D. However, the government licensed them to practice, and the majority settled in smaller cities or larger villages. They proved a useful group. At the present time the government has ruled that all schools shall upgrade and prepare to give full training or close.

It can easily be seen that there is a large medical vacuum which is filled in various ways.

Besides the system of western medicine there are indigenous systems. One is Ayurvedic medicine. This is apparently Persian in origin and is embalmed in the Vedas. It has its own pharmacopea of native drugs and herbs. It is a strange

mixture of religion, superstition, magic and empiricism. Many of the drugs are undoubtedly of some efficacy, especially those for the treatment of the prevalent dysenteries and worm diseases. They are cheaper, though less effective, than most western drugs.

Another system, Unani, is Greek medicine introduced by the Arabs. It might be likened to a fossil of the base on which western medicine developed.

There are schools where these systems are taught, and along with the extreme nationalism and reaction against anything western, which is prevalent in India today, there is a movement to decry western medicine and to emphasize the native systems. This has resulted in some of the state schools having departments of both systems. For instance, in Mysore the government medical school has two hospitals. Western medicine is practiced in one. Above the door of the other is announced that it is a hospital for Ayurvedic and Unani. The two buildings are on opposite corners and are equally imposing. There is at least one school posing as an Ayurvedic school which is really a school of western medicine with a subordinate department of Ayurvedic.

Homeopathy has some following, and I am told that a six month's course results in a license to practice. Great stress is laid on the theory of potencies and on "Similis similibus curantur."

There are hakims and vaids who have no training in science, but whose art is passed down from father to son. They have some knowledge of the action of indigenous fruits, herbs, leaves and roots, some "English" drugs, such as belladonna, cannabis indica, nux vomica, sodium bicarbonate, potassium iodide and opium, which can be bought in the bazaars all over India.

In the past many "dispensers" or pharmacists have been licensed and have practiced in the villages. On the whole this has probably been a useful group. They know something of drugs, and if they have a reasonable amount of intelligence certainly must learn from experience what to do for the great curses of the Indian villages—malaria, amoebic and other dysenteries, worms and conjunctivitis.

In addition to these more or less "regular" practitioners are the quacks of various kinds. Some in the more isolated villages may through experience become useful. However, many are vicious and harmful. A striking example of the latter are the "couchers" who go among the villages treating cataracts. With a needle they loosen the lens and push it back into the vitreous. This gives immediate restoration of vision. However, in ninety percent of cases irremediable blindness results within three years and in some cases within a few hours. The lens acts as a foreign body and may cause panophthalmities. Recently, I heard of a "school" where in a course of two weeks the techniques of couching and of the injection of penicillin is given.

Obstetrics in the villages is largely in the hands of untrained midwives or of the neighboring women who have little conception of asepsis and no knowledge of the way to handle abnormalities. Consequently, maternal and infant mortality are high. The prejudice against men attending women is gradually breaking down,

but it is still an advantage to have a woman in charge of this branch. Two of the mission schools, which, until just recently have taken only women as students, were founded to meet the demand for women doctors. The Lady Harding School in Delhi is also a medical college for women.

Surgery in the villages is largely that of wounds and fractures and may be very crude. I saw one boy whose arm had to be amputated in the mid-humeral region, one whose hand had to be amputated, and another whose hand was rigid and ischaemic. All were due to mistreated fractures.

In the colleges surgery is well taught, and the standard of Indian surgery in the cities is high. I have attended two sessions of the India Surgical Society and have been impressed with the calibre of the men and the papers presented. The papers are all in English, for the members come from all parts of India and all the major languages are represented.

Abdominal and pelvic surgery seems to be well handled. A good deal of lung surgery is done. I have not heard of any heart surgery, but at the last meeting of the Surgical Society a movie of a mitral valvectomy was shown. I suspect that such operations will soon be attempted. Neurosurgery is a new field, but there are outstanding neurosurgeons in Vellore and Bombay and probably in Calcutta.

There are numerous orthopedic men, and there is plenty of work for them for the results of poliomyelitis and of mistreated trauma can be seen on driving through any village. Urology is not yet a specialty, and a cystoscopic examination is treated as a major procedure.

Tropical and parasitical diseases are well known and well treated. One of the worlds outstanding schools of tropical medicine is in Calcutta.

Xrays are common, but unless subsidized by government or mission they are beyond the reach of the poor. Where a coolie's daily wage is a rupee and a half, and the cost of an Xray is twenty rupees, the problem is obvious. Pictures are often made on photographic paper, but such are of limited use. Deep Xray therapy is used in many places, and a supply of radium is possessed by a few hospitals.

The newer antibiotics are available pretty generally and are used even by the Ayurvedic physicians. Penicillin is used freely and is often given free, but the others are expensive.

Now for a few of our own personal experiences and observations in India. In the region where we are stationed, insects are not a problem. In the year and a half we have been here we have not slept under mosquito nets a half dozen times. However, we use nets when we travel in hot weather or in moist areas, especially when we sleep in unscreened traveller bungalows. We also take with us prophylactic camoquine. We have not seen malaria except in the chronic state with the large spleen and that from outside our district which is dry and free from the disease. Our visits have taken us to regions where the rainfall is heavy. These areas which formerly suffered greatly from malaria are now almost free as a result of the use of D. D. T. supplied by the government.

The chief curse of our region, and I believe of all India, is the amoeba. The infestation rate is high, and I understand that all westerners are infected sooner or later. We were both infected in our first year. I was the first, and for three months was under par. My wife was more seriously affected, for she had hepatitis and was in bed for three months. All of us are careful about boiling our water and milk and avoiding uncooked foods. In spite of this, more westerners are invalided home because of the amoeba than for any other cause.

We see typhoid, paratyphoid and cholera in the hospital but no plague. The mortality of cholera is high, for most cases come to us in the late stages. We take the cholera vaccine every six months, and, so far, I have not heard of anyone so protected who contracted the disease. As soon as a case of cholera occurs in a village the government sends officials there with vaccine. There have been no great outbreaks in recent years. The times of the pilgrimages are most feared. People come from all parts of the country. The trains are crowded (at the Kumbh Mela I saw people riding on the roofs of the cars). One sick pilgrim has the opportunity of distributing his faeces over a large area. Typhoid seems to yield to the antibiotics, and we have seen no typhus.

I have seen a few cases of elephantiasis, none of acute filiariasis, one case of Madura foot, one of Guinea worm with calcified tract, and on one of my trips a case of Kala Azar. Worms, especially round worms, are very common, and in any village children with protuberant bellies are seen running around. Hook worm is a problem in the south.

A severe form of conjunctivitis is seen in the villages, which is probably due to dust, and which causes much blindness from the resulting corneal ulcers. The most heartbreaking sight I have seen was an eighteen month old baby crying because of pain in his eyes. Both corneas were completely and acutely ulcerated away. I am told that there is a form of glaucoma caused by the use, in some places, of a cheaper substitute for mustard oil for cooking. Cataracts are common—more so in some parts of the country than others.

Some of the well known ophthalmologists organize "eye camps" in strategically placed villages. Cataracts are treated on an assembly line basis, and an unbelievable number of operations are done in a day. The best known ophthalmologist on the mission field told me that his personal record was eighty-five operations in one day, and I have heard of other high records. The results are exceptionally good.

Tuberculosis, undernutrition and malnutrition are seen everywhere. I think it is fair to say that most of our patients are undernourished. It is said that in India forty percent are adequately nourished, forty percent are undernourished and twenty percent hungry.

I do not know what the average hemoglobin percent is, but I have come to consider sixty percent good when operating is concerned, and am willing to operate if the hemoglobin is fifty percent. I saw one woman with a percent of eighteen go safely through caeserian section. Ascites is often seen, and cirrhosis of the liver frequent.

At the hospital we see an occasional leper. A mile away and under the supervision of the hospital group there is a lepresarium with two hundred of these unfortunate people. There are said to be between one and two million lepers in India and too few institutions for their care. They gather into groups, more or less pariahs, have their own officers and special laws, and form a kind of nation within a nation. Begging is their chief source of livelihood.

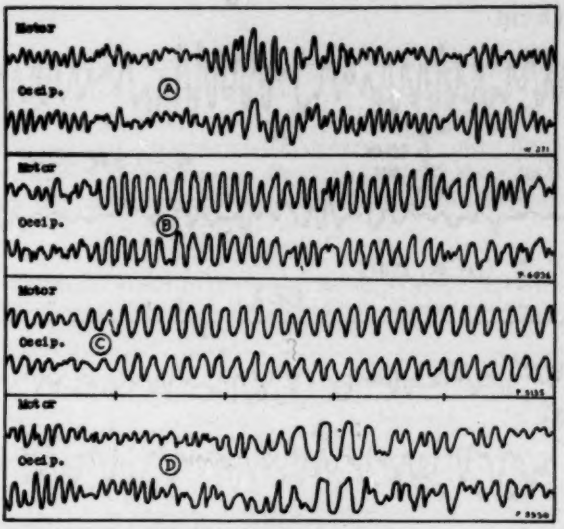
The medical and health problems of India are staggering; however, the government is making heroic efforts to meet them and with some success. It seems fair to say that health conditions show steady improvement. This is borne out by a ten-year increase in life expectancy in the last twenty years.

Health, food and education are all part of the problem. The plan of sending to the villages men and women with some training in fields such as sanitation, agricultural methods, and domestic science is an attempt by the government to partially meet these needs. The Ford Foundation is taking an important part in this plan as well as one of the missionary institutions and the agricultural college at Allahabad.

# THE RESEARCH ASPECT OF THE EPILEPTIFORM SYNDROME

LORNE D. PROCTOR, M.D.*
ROBERT S. KNIGHTON, M.D.**

During the Second Great War, routine electroencephalograms done on members of the Royal Canadian Air Force revealed that 10-15 out of every 1000 (approximately 1 percent) showed electro-cerebral activities indistinguishable from those associated by Gibbs et al with psychomotor epilepsy Fig. 1 and Fig. 2. This group




Elements of Psychomotor Patterns

Fig. 1

of individuals certainly represented an above average sample of the general population. Their records showed no physical or psychiatric abnormalities. Many were re-interviewed by a psychiatrist and/or neurologist. There was only one in a group of over 2000 who gave a history of attacks which in any way resembled psychomotor states. Goodwin[1] reported the findings in the electroencephalograms. He noted that the slow square topped waves were occurring at exactly one-half, and the fast variant at double the concurrent alpha rate. Typical examples of the slow and fast variants are shown in Fig. 3.

Then 550 presumably normal individuals were chosen at random. These did not have the thorough screening utilized by the R. C. A. F. group. It was found that the recordings of 10 percent of these subjects contained traces or more of

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**Chief, Division of Neurosurgery.

the alpha variants. Subjects showing alpha variants were thoroughly examined, and those having clinical signs or symptoms associated with the EEG changes came under the broad headings of psychoneurotics and/or epileptics.

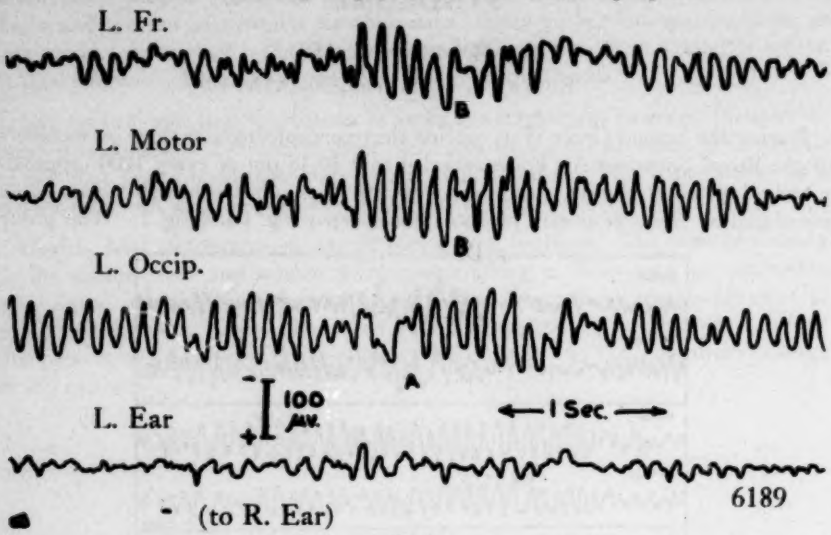



Fig. 2

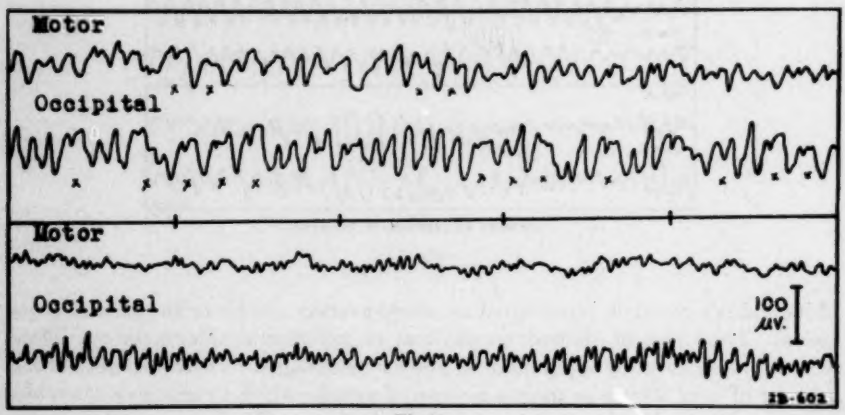



Fig. 3

Table 1 shows the percentage of the patients in these groups demonstrating alpha variants in their EEG. It was not surprising to find 73 percent of epileptics with this EEG abnormality, but we did not understand the high incidence in the psychoneurotic group.

After some 12 years of observation the so-called psychoneurotics in this group proved to have developed episodic disorders, 95 percent of which had varying degrees of impaired consciousness. Several intractable migraine cases in the group responded to appropriate anti-epileptic therapy.

TABLE 1

INCIDENCE OF THE ALPHA VARIANTS (FAST AND SLOW) IN THE ELECTROENCEPHALOGRAMS OF VARIOUS POPULATIONS

| GROUP | NO. OF CASES | PER CENT WITH ALPHA VARIANTS |
|---|---|---|
| SELECTED NORMAL | 550 | 10% |
| PSYCHONEUROTICS* | 94 | 45% (P < .01) |
| EPILEPTICS* | 134 | 73% (P < .01) |

*FINAL DIAGNOSIS.

There have also been several cases of fugues or compulsive behaviour which one would expect in psychomotor attacks. The psychoneurotic features in many cases were either initiated by or contributed to through an episodic impaired consciousness which produced understandable anxiety. This often disappeared under appropriate anti-epileptic medication. Proctor[2] reported the response to sodium dilantin, sodium amytal and phenobarbiturate, singly or in combination (Table 2).

TABLE 2

CLINICAL RESULTS (Preliminary Report November 28, 1946)
Response of 132 patients with psychomotor syndrome to various types of medication.

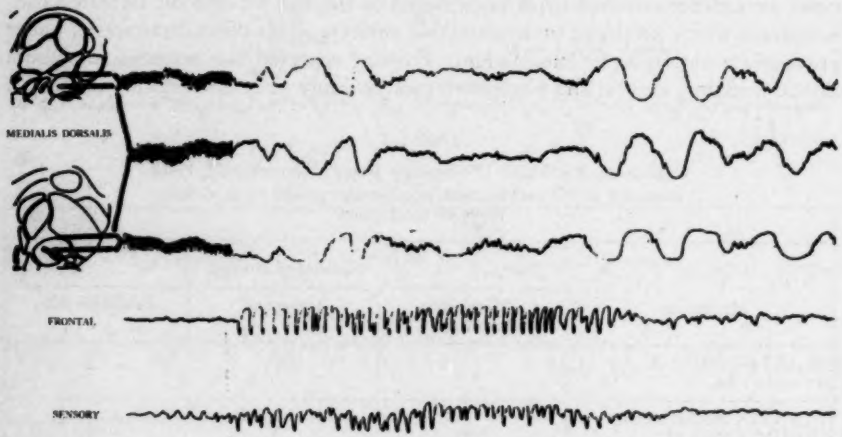
| Medication | Number of Patients | | |
|---|---|---|---|
| | Markedly Improved | Improved | Unimproved |
| DILANTIN SODIUM (see notes 1 and 2) | 27 | 10 | 5 |
| DILANTIN SODIUM plus SODIUM AMYTAL | 2 | 3 | 0 |
| DILANTIN SODIUM plus PHENOBARBITURATE (see note 3) | 32 | 14 | 1 |
| PHENOBARBITURATE | 1 | 7 | 14 |
| SODIUM AMYTAL | 0 | 7 | 9 |

Note 1: 4 cases in this group may have had grand mal attacks.
Note 2: Drug withdrawn in 7 cases. All 7 patients relapsed.
Note 3: 80% of this group are mixed psychomotor-idiopathic grand mal. None are purely idiopathic grand mal.

It is noteworthy, that the patients responded selectively to sodium dilantin and showed a very poor response to sodium amytal or phenobarbiturate. The latter two drugs should have been beneficial if we had been dealing primarily with a psychoneurotic syndrome. In discussing our findings with Dr. Wilder Penfield in 1947, he agreed that we may be dealing with the phenomena which Gowers[3]

described in 1907 as the borderlands of epilepsy. Also he agreed that the term epileptiform syndrome was as suitable as any for this phenomena.

As our series has enlarged, we have been more and more impressed with the predominance of impaired consciousness in the patients' symptomatology. We have been unable to produce consistently the alpha variants by stimulation through scalp electrodes in the human. We have, therefore, embarked on an investigative problem using monkeys (Macacca Mulatta), endeavoring to determine the site in the brain or brain stem which might produce this episodic impairment of consciousness and concurrent alpha variant activity at the cortex of the brain. Dr. R. S. Knighton has very kindly collaborated in this aspect of our research. It was a happy coincidence that while working at the Montreal Neurological Institute, he had noted alpha variant activity occurring at the cortex on stimulating the hypothalamus of cats (Fig. 4). It was not possible to measure critically changes in consciousness in the cat at a time when the animal was under nembutal sedation.



STIMULATION OF HYPOTHALAMUS IN REGION OF LATERAL NUCLEUS AND MEDIAL FOREBRAIN BUNDLE. SECTION OF THALAMUS AT FRONTAL PLANE 11.

H.L. lateral nucleus of hypothalamus
MFB medial forebrain bundle
H.P. posterior nucleus of hypothalamus

Fig. 4

In the past year a primate laboratory has been established at the Henry Ford Hospital, and we are gradually solving the technical problems in the production of an efficient intra-cerebral electrode. At present we are using a glass-covered, enameled, stainless steel wire No. 50, the enamel being scraped off for about 2 mms. from the tip of the electrode.

The matter of evaluating minimal changes in consciousness presented a problem, and we have to thank Dr. Harry Harlow of the University of Wisconsin who kindly arranged the training of one of our psychologists in psychometric testing of monkeys.

The monkey is tested for some months until a plateau of performance is established. Then, the animal is tested before and after the stimulation by the implanted electrode and comparison of his performance prior to and immediately following stimulation used as a measure of impairment of consciousness.

The accurate placement of electrodes intra-cranially is technically difficult, but Dr. Knighton, using a Horsley-Clarke sterotaxic unit, is most proficient.

We obtain confirmation of the actual location of the electrode by means of Xray and finally by coagulation at the point of the electrode, sacrificing the animal and perfusing with ferro cyanide solution to mark where the point of the needle has deposited iron on coagulation.

The animal on which we are presently working appears to have the electrode placed in the mid-brain. On stimulation, which requires a very small potential of approximately 2/10 of a volt, the head and eyes deviate to one side. The pupils contract or dilate (depending upon the polarity), and, finally, the animal emits a short cry on termination of the stimulus.

The EEG from this area shows the expected 5 to 6 per second high voltage activity. We have not been able to discern any change in this activity beyond 20 seconds after stimulus with the above voltage for approximately 2 seconds.

We believe there is a slight impairment of consciousness following the stimulus that lasts for approximately 2-3 seconds. We have yet to obtain a record from scalp electrodes in the occipital and temporal regions during the period of stimulus, as we have not produced other than an efficient monopolar electrode. We feel that at least a bi-polar electrode for proper stimulation in this area of the brain to drive the appropriate areas of cortex will be necessary.

We have endeavoured to set out the nature of our research in this problem, and feel that it should throw some light on these borderline epileptic states which we have called epileptiform syndromes. We have in mind to explore the results of stimulation of the various reticular formations within the brain, hoping that this will help us to understand better the role this formation plays in the state of consciousness. We believe epilepsy is not a well defined state, and this syndrome enlarges our conception of its limits.

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# NEWER OPIUM ANTAGONISTS, THEIR ACTIONS AND USE

PAUL R. DUMKE, M.D.*

Early in the history of medicine, opium was found to be a reliable and potent agent for the relief of pain. Through purification morphine has become popular as a potent and superior analgesic agent. Morphine and all of its derivatives are effective because they elevate the pain threshold, produce sleep, alleviate fear and produce relaxation. Respiratory depression and not infrequently circulatory depression are not uncommon when these drugs are exhibited in an attempt to attain maximum therapeutic effect and are a most dangerous symptom of opiate intoxication. These deleterious effects have in many instances precluded their use in geriatric, pediatric and obstetric patients.

Demethylation of morphine, codeine and other related alkaloids diminishes their analgesic potency. In 1915 Pohl[1] by substitution of an allyl for a methyl group in codeine, produced a compound called N-allylnorcodeine that counteracted to some extent the respiratory depressant effect of morphine. McCawley, Hart and Marsh[2] in 1941 substituted an allyl for a methyl group in morphine. This compound known as N-allylnormorphine was shown to have marked stimulatory effects on respiration and circulation in animals depressed by morphine. In 1943 Unna[3] reported its use in antagonizing the effects of morphine injected into mice. The data remained in the literature as a pharmacological curiosity until 1952 when Eckenhoff, Elder and King[4] reported the use of N-allylnormorphine in the treatment of morphine and demerol narcosis and overdose.

N-allylnormorphine is structurally identical with morphine except for the replacement of a methyl group. (Fig. 1) Meperidine is structurally different from morphine when the formula is written on paper, and the relationship between the two molecules is obscure; but when three-dimensional models are constructed there is a close similarity of pattern, so we can expect N-allylnormorphine to antagonize meperidine. Recent clinical studies have shown N-allylnormorphine to be effective against depression produced by dilaudid, metapon, methadon, morphine and meperidine.

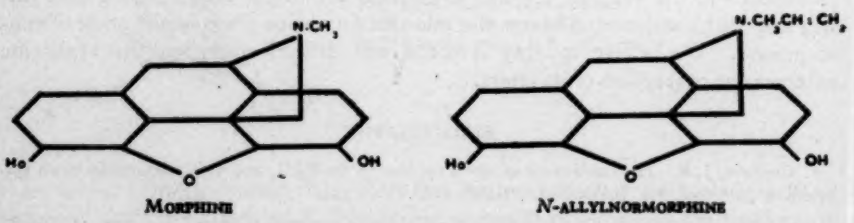


Fig. 1—Outline diagrams of molecules of morphine and nalorphine.

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N-allylnormorphine is quite interesting. Injected intravenously into a normal unpremedicated individual, it acts as a respiratory and circulatory depressant. Evidence presented by Tenney et. al.[5] points to the fact that N-allylnormorphine changes the threshold response of the respiratory center to carbon dioxide tension or pH. The sensitivity of the respiratory center is lowered by approximately 50 percent.

When the drug is injected into man, prior to the administration of a large dose of morphine, it inhibits the respiratory and circulatory depressant actions of the opiate; injected into a patient narcotized from large doses of the opiates, it causes a strong respiratory stimulation as well as a moderate circulatory stimulation. In spite of the stimulatory actions following opiate depression N-allylnormorphine seems to do little to counteract the sedation and analgesia produced by the opiates.

Injection of N-allylnormorphine into a subject deeply narcotized by morphine or any of its derivatives produces a dramatic effect as far as respiratory stimulation is concerned. The respiratory stimulation when 5 mgm. of the drug is exhibited intravenously in a patient narcotized with 60 mgm. of intravenous morphine is striking. The deep slow respirations that characterize opiate poisoning abruptly change after the antagonist is exhibited. In 15 or 20 seconds respiratory rate is increased 3-4 fold with regular less deep breathing. The change is not gradual as one sees after picrotoxin antagonism of barbiturate intoxication, nor is it an intense stimulation such as that seen with nikethamide or metrazol. Intense stimulation and then the gradual decline in respiratory rate and minute volume is not a characteristic of the new antagonist.

The effect of the antagonism on the circulation of the narcotized patient is not dramatic. If the blood pressure is depressed, it returns toward normal levels. If the pressure is normal the drug causes no marked change. The pulse rate is uniformly slowed.

The site of action of N-allylnormorphine has not been defined, but it is probably central. It may act in a competitive fashion with the opiates for certain receptors on cells of the central nervous system. It is possible for the drug to either occupy the receptor and block the action of the opiate, or it may displace the opiate. This is probably a nonspecific action because the sedative effect of the opiate is not blocked or completely displaced.

Another drug capable of the same effects against some of the opiates is levallorphan tartrate (3-hydroxy-n-allyl-morphinan). It bears a relationship to dromoran similar to that of N-allylnormorphine to morphine. It is an effective antagonist against respiratory depression produced by dromoran, nisentil, morphine, and demerol. Here then, we have two drugs which can be used intravenously to combat toxic effects of narcotics.

Some anesthetists have been using these drugs prophylactically in an attempt to eliminate the respiratory depressant and hypotensive effects that intravenous opiates possess. Obstetricians are using the drugs prior to delivery of an infant from a mother who is unduly depressed by opiates.[7] The respiratory depression in the newborn due to placental transfer of opiates is prevented by the antagonists.

The drug may also be given in 2 mgm. doses directly into the infant's umbilical vein if the depression of the newborn is thought to be due to opiates. Used this way the analeptic effect is quite dramatic.

It is important to remember that these drugs have no effect on depression of circulation or respiration caused by the barbiturates or any of the anesthetic agents. They are specific antagonists of opiates. N-allylnormorphine or levallorphan in persons not under the influence of narcotics produces lethargy, mild drowsiness, vivid daydreams, and dysphoria varying in intensity from vague anxiety to acute panic. All subjects complained of inability to repress such daydreams.

Of course, it goes without saying that these two drugs are life saving in the presence of severe opiate overdose, be it self-induced or accidental. The drugs are specific and are used in a 10 mgm. dose intravenously after the usual clear airway and adequate oxygenation of the patient is obtained. Repeated injections of the drug every 4-5 minutes, until 60 mgm. or more have been given, may be required to effect a stimulation of respiration and circulation in a severely poisoned individual.

It would be interesting to know what specific structural unit of N-allylnormorphine and levallorphan causes the antagonism of the opiates. If such a unit is found the chemists might be able to synthesize drugs which could have the same effect of antagonizing the respiratory depressant effects of barbiturates or cyclopropane.

Progress is being made in this direction. A wide number of drugs have been reported to have analeptic properties against the opiates. All of these analeptic drugs have either a muscarine like action or are anti-choline esterase drugs. A common chemical link in all of these drugs is a 2-4 diamino 5 phenyl thiazole.

When drugs with this linkage were tried against barbiturate intoxicated dogs they were roused. A report of successful trials in animals and in 20 cases of barbiturate poisoning in man of a new drug incorporating the 2-4 diamino 5 phenyl thiazole linkage[8] has recently been made. This may be the linkage which is common to analeptics of this type. It will be interesting to see if the specific structural

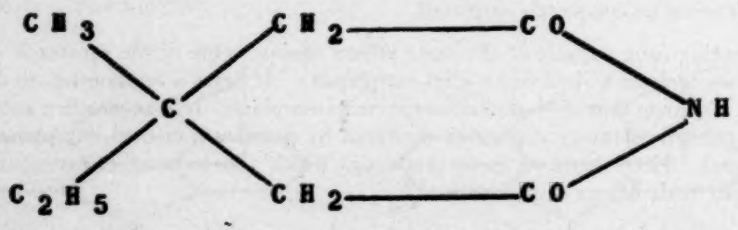


Fig. 2—bb METHYL ETHYL GLUTARIMIDE
(N P 13)

unit can be isolated and used successfully. The barbiturate antagonist increased respiration and as the dose was increased produced wakening. If the drug is used in normal subjects it produces convulsions which can be controlled with barbiturates. The new drug (Fig. 2) is designated N P 13. Chemically it is bb methyl ethyl glutarimide and is quite specific against barbiturates.

The opiate antagonists are proving their usefulness everyday. Barbiturate antagonists with as much specificity as N-allylnormorphine would be a great advance in treatment of barbiturate toxicity.

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# THE HYPONATREMIC SYNDROME

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The hyponatremic syndrome is a phenomenon of recent reported prevalence, perhaps largely due to the facility with which sodium determinations can be performed by the flame photometer in the last decade. The low sodium syndrome or less specifically 'the low salt syndrome' are terms used synonomously. Related to this syndrome are the former descriptions of "hypochloremic azotemia" and also the syndrome of "water intoxication."

The term hyponatremic syndrome implies that there are clinical signs and symptoms which are rather specifically related to a low sodium concentration in the serum and extracellular fluid. In recent years, a low sodium concentration has been found frequently to accompany a wide variety of diseased states. This has led to some confusion about the syndrome, since many of the symptoms and signs may be associated with the primary diseases and not necessarily with the incidental finding of low sodium concentration. Thus the specificity of the clinical symptoms and signs needs careful analysis. If a definition of the syndrome is to be useful, one might hope to develop accurate diagnosis and treatment which would correct specifically the manifestations. Let us approach the problem of definition.

The term low salt syndrome was first popularized by Schroeder in describing some patients with cardiac failure and edema with low serum sodium concentrations. Even though the name of the syndrome seemed to put emphasis on sodium, Schroeder stated plainly that this condition could be brought about by dilution of electrolytes from a *high water* or low salt intake. Thus he might just as well have called it the 'salt dilution' syndrome. He postulated that this condition followed the use of mercurial diuretics in conjunction with diets low in sodium chloride and that the administration of concentrated sodium chloride was sometimes corrective.

The dictionary says that the word syndrome means 'concurrence,' and when used in medicine it is "a group of signs and symptoms that occur together and characterize a disease." The definition of the hyponatremic syndrome needs clarification in at least four important ways.

*Emphasis on regulation of water as well as sodium concentration.*

If the sodium concentration is abnormally low, the water concentration is abnormally high. Equal emphasis upon water and sodium is important because from the standpoint of etiology it is apparent that the abnormal concentration could be produced either by a loss of sodium or by a gain of water in the extracellular fluid compartment or by both. There is perhaps a tendency today among clinicians to lay the blame on the sodium ion and proceed with therapeutic manipu-

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lation of sodium intake at the same time adhering to the therapeutic principle of water intake being forced or given ad libitius. We must look with suspicion upon the mechanisms for regulation of water as well as for sodium metabolism.

*The problem of internal intercompartmental sodium and water balance regulation.*

Secondly, the terms "low" or "high" do not specify in what part of the body sodium and water are increased or decreased. It is conceivable that a low concentration, without alteration in total body content, could be produced by a shift of sodium into cells and/or shift of water out of cells. In addition, the size of the intravascular compartment or the blood volume may be important in the production of some of the circulatory abnormalities of the syndrome. We must examine the mechanisms responsible for the balance of electrolyte and water across the internal boundaries; namely, the capillary and the cell walls. This may be called the problem of internal intercompartmental balance regulation.

*Importance of other electrolyte abnormalities.*

Third, we have a problem of defining whether certain clinical signs and symptoms are specifically related to alterations in sodium concentration. In many of the diseases accompanied by low sodium concentration there may also be a derangement of potassium concentration and frequently a depletion of intracellular potassium. In some cases we might reasonably ask if abnormalities of other electrolytes, for example, of magnesium, may be responsible for some of the symptoms. Furthermore, parts of the clinical picture may be modified by the relative concentrations of chloride to sodium and by the presence of acidosis or alkalosis. All electrolyte abnormalities which accompany the hyponatremia must be examined.

*External body sodium and water balance regulation.*

Fourth and last, the description of any hyponatremic situation should include knowledge concerning the direction of external total body sodium and water balances. Some patients with hyponatremia can excrete administered sodium and water normally, others cannot. It is not enough to know only how much or how little sodium and water is being excreted by the kidneys or lost by other routes. We must know what proportion of the intake is being lost. We cannot determine by analysis of serum sodium concentration alone how the over-all regulation of body sodium or water balance is being conducted. A few determinations of total dietary intakes and total urinary sodium and water outputs are worth more than several serum concentration determinations when managing the patient. Estimation of water balance may be more difficult than of sodium because of variation in insensible water loss; but it is nonetheless important in determining the picture.

In Table I is summarized the points so far considered important when describing any hyponatremic situation.

TABLE I

External Total Body Balance Regulation of Sodium and Water

a) Influence of magnitude of intake

b) Renal control of excretion
c) Insensible loss and loss by G.I. tract

TABLE II

Internal Intercompartmental Balance Regulation of Sodium and Water

1. Intravascular ⟷ Extravascular, Extracellular
   a) Hydrostatic capillary pressure
   b) Tissue pressure and elasticity
   c) Serum protein concentration
   d) Blood loss
2. Extracellular ⟷ Intracellular
   a) Cell energy and osmotic control
   b) Influence of hormones
   c) Malnutrition
   d) Acid base balance
   e) Anoxia (?)

TABLE III

Associated Electrolyte Derangements

a) Potassium
b) Chloride
c) Magnesium (?)
d) Metabolic or Respiratory acidosis or alkalosis

The factors involved in the regulation of internal intercompartmental, and of external balance are listed, as well as possible associated electrolyte abnormalities. Of course, it is much easier to list these factors in a table than to determine them in each case.

In the remaining time, I shall attempt to outline the clinical physiological pathology of the hyponatremic edematous cardiac patient, drawing a little from my own experience, and using as much information as I could find from the work of students on this subject. The factors are summarized in Tables A through E.

"HYPONATREMIC SYNDROME"
of the
Edematous Cardiac Patient

A. *CLINICAL FEATURES:*

1. Older patient
2. Severe failure
3. Prolonged failure
4. Poor prognosis
5. Cirrhosis of liver (cardiac)
6. Inelastic tissues
7. Previous low sodium diets
8. Previous mercury diuresis
9. Malnutrition
10. Water given—forced or ad lib

### B. *PHYSIOLOGICAL FEATURES:*

1. Low serum sodium concentration
2. Low serum chloride concentration (Metabolic alkalosis)
3. Azotemia progressive
4. Low serum proteins
5. Water antidiuresis
6. Sodium antidiuresis
7. Cell potassium decreased
8. Total nitrogen deficit
9. Cell sodium increased
10. Cell water increased
11. Abnormal thirst mechanism
12. Low blood pressure (peripheral circulatory insufficiency)

### C. *SYMPTOMS:*

| *Non-specific* | *Specific* |
|---|---|
| 1. *Weakness, Drowsiness, Lethargy,* Apathy | 1. Thirst |
| 2. *Anorexia, Nausea, Occasional vomiting* | 2. Muscular and abdominal cramps |
| 3. Mental confusion, Psychosis, Coma | 3. Convulsions, Twitchings |

### D. *RESPONSE TO THERAPY:*

1. Unresponsive to sodium restriction
2. Unresponsive to more digitalis
3. Aggravated by excess water intake
4. Unresponsive to mercury *or*
5. Mercury diuresis of potassium with chloride (low potassium toxicity occasionally)
6. Thirst with water restriction
7. Thirst with sodium administration
8. Rise in serum sodium without diuresis on administration of large doses of potassium

### E. *RESPONSE TO CONC. NaCl ADMINISTRATION:*

1. Usually disappointing, no diuresis
2. Demonstrates large sodium space (cellular plus extracellular)
3. Mercury responsiveness (?) Increased diuresis due to excess available chloride
4. More edema (if water not restricted)

There are many other situations besides the edematous cardiac patient in which hyponatremia occurs. Each of these situations must be characterized in terms of the internal and external balance behaviour. The many situations are listed in Table F., and many have been studied extensively with experimental and clinical methods.

### F. *OTHER HYPONATREMIC SITUATIONS*

1. Tuberculosis
2. Malnutrition
3. Hypoadrenalism
4. Post-operative overhydration

5. Hypodermoclysis overhydration
6. Heat cramps—water intoxication
7. Gastrointestinal salt loss
8. Nephrosis
9. Cirrhosis of liver
10. Hypoalbuminemias
11. Pitressin administration
12. Renal disease—salt loss
13. Miscellaneous injuries and illness
14. Experimental dialysis

*CONCLUSION:*

The hyponatremic syndrome of the edematous cardiac patient is caused primarily by a failure of the mechanisms for maintenance of proper proportions of sodium, chloride, potassium and water in all body fluid compartments. Its onset is accelerated by low sodium diets, mercurial diuretics and high water intake. The mechanisms failing are those that selectively control intake, namely thirst and appetite, those that control selective renal excretions, and those which preserve the internal structure of cells.

No ready solution to the problem and no therapy which is specific can be offered. The best treatment is to avoid it. Many cases are irreversible and represent in the patient with cardiac failure a final dissolution of the mechanisms for regulating body fluid structure.

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(Abstract)

# HORMONES OF THE POSTERIOR PITUITARY

VINCENT DU VIGNEAUD, Ph.D.*

THE EDSEL B. FORD LECTURE, 1954

Since the discovery of the blood pressure-raising activity of extracts of the posterior pituitary gland by Oliver and Schafer in 1895, numerous biological activities have been found to be associated with this gland. These include the contraction of the uterus—the so-called oxytocic action, noted by Dale in 1905—the antidiuretic activity, the milk let-down activity, and the avian vasodepressor activity. With the knowledge of these actions, it became of considerable interest to determine the nature of the active principle or principles in the posterior pituitary.

Beginning with the early part of this century, attempts were made by various investigators to isolate the principle or principles in pure form. In the late 1920's Kamm and co-workers effected extensive purification of the posterior pituitary material and were able to obtain fractions highly potent in pressor activity with very little oxytocic activity and *vice versa*.

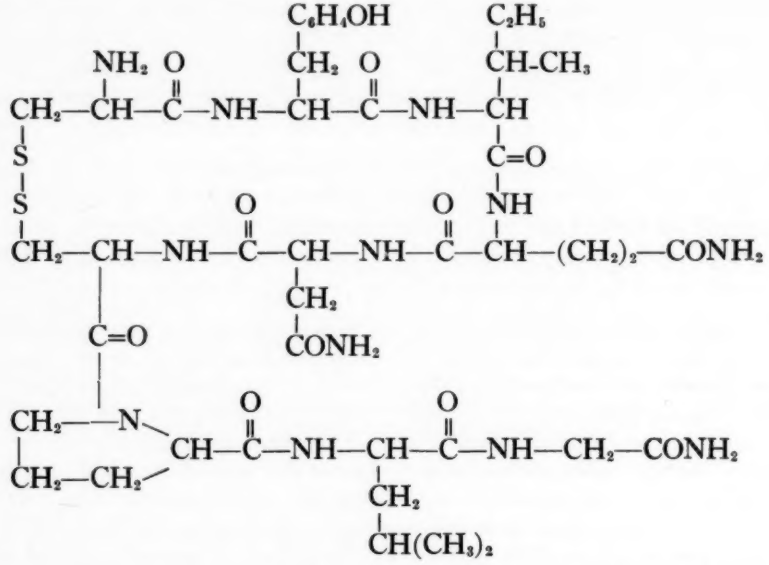
The studies carried out by the author and his associates on the posterior pituitary hormones date back to 1932, when these hormones were studied as an outgrowth of some researches on the chemistry of insulin. The methods employed in the studies prior to 1942 involved mainly electrophoretic techniques and those in the later studies, countercurrent distribution. As a result of the countercurrent distribution studies, highly purified preparations of the oxytocic hormone, oxytocin, and the pressor-antidiuretic hormone, vasopressin, were obtained. The oxytocin was obtained in crystalline form as a flavianate, representing the first isolation of this principle as a crystalline derivative. Hydrolysis of oxytocin showed it to contain eight amino acid residues, namely leucine, isoleucine, tyrosine, proline, glutamic acid, aspartic acid, glycine, and cystine, in equimolar ratios to each other and ammonia in a molar ratio of three to any one amino acid. Vasopressin from beef glands was shown to have the same constituents except that leucine and isoleucine were absent and phenylalanine and arginine were present. The vasopressin isolated from hog glands was found to differ from that isolated from beef glands in that the hydrolysate contained lysine in place of arginine. No difference was detected in the oxytocins derived from beef and hog glands.

With these purified preparations, it has been shown that oxytocin possesses oxytocic activity on the isolated rat uterus, avian vasodepressor activity and a highly potent milk-let-down activity. It has also been demonstrated that this preparation of oxytocin possesses slight but definite pressor and antidiuretic

*Professor of Biochemistry, Cornell University, Medical College. Read before the Henry Ford Hospital Medical Society, Nov. 9, 1954.

activity. The vasopressin possesses both pressor and antidiuretic activities. In addition, vasopressin has been shown to possess milk-let-down activity, avian vasodepressor activity, and oxytocic activity to a considerably less degree than that exhibited by oxytocin.

After the determination of the amino acid composition, the next step was to find out how the individual amino acids and ammonia were linked together to form the respective hormones. Degradative studies of oxytocin, including oxidation with performic acid, desulfurization with Raney nickel, determination of terminal groups, cleavage with bromine water, determination of sequence of amino acids by Edman degradation and partial hydrolysis with acid, led to the postulation of the following structure for the hormone.



Degradative studies on arginine-vasopressin resulted in the postulation of a similar type of structure for arginine-vasopressin, with phenylalanine replacing isoleucine in the ring and arginine replacing leucine in the side chain. The work on lysine-vasopressin indicated that it possessed a structure parallel to that of arginine-vasopressin, with lysine replacing arginine in the side chain.

As the final step in the determination of the structure of oxytocin, its synthesis was undertaken. This was accomplished by coupling N-carbobenzoxy-S-benzyl-L-cysteinyl-L-tyrosine with the heptapeptide amide L-isoleucyl-L-glutaminyl-L-asparaginyl-S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycinamide, prepared in turn from tosyl-L-isoleucyl-L-glutaminyl-L-asparagine and the tetrapeptide amide S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycinamide; the resulting protected nonapeptide amide was reduced in sodium-liquid ammonia and converted to the cyclic disulfide by aeration in aqueous solution. The synthetic octapeptide amide was compared with natural oxytocin as to potency, specific rotation, partition co-

efficients, amino acid composition, electrophoretic mobility, infrared pattern, molecular weight, enzymatic and acid inactivation, chromatography on the resin IRC-50, and cleavage with bromine water. The synthetic material and natural oxytocin were also compared with respect to milk ejection and induction of labor in the human as well as rat uterus contraction *in vitro*. Crystalline flavianates prepared from the synthetic material and from natural oxytocin were found to have the same crystalline form, melting point, and mixed melting point. All of these comparisons afforded convincing evidence of the identity of the synthetic product with natural oxytocin. This synthesis thus constitutes the first synthesis of a polypeptide hormone.

Comparable approaches to the synthesis of lysine-vasopressin and arginine-vasopressin have yielded encouraging results.

# THE DIAGNOSIS OF HEPATIC PATHOLOGY BY NEEDLE BIOPSY

ROBERT J. PRIEST, M.D.,* WAYNE L. AGEY, M.D.,** HUGH H. STEELE, M.D.,*** and JEROME W. FISCHBEIN, M.D.****

Needle biopsy of the liver has proved to be a valuable technical advance in the diagnosis of hepatic pathology. As Zamcheck and Sidman[1] recently have pointed out, "it is not necessary for the correct diagnosis of most cases of liver disease." However, the precise usefulness of this technique is now apparent. There have been over 20,000 biopsies reviewed in the literature.

## INDICATIONS

The indications for needle biopsy of the liver may be outlined as follows:

1. To define the stage of known liver disease for treatment and prognosis.
2. To diagnose certain hepatic pathologies in which examination of the tissue is indispensible, e.g. hemochromatosis, glycogen storage disease.
3. To disclose the presence of systemic disease in the liver.
4. To investigate and understand the pathogenesis of clinical liver disease.

## OBSERVATIONS

In the past four and one-half years at Henry Ford Hospital 260 needle biopsies of the liver have been done in 250 patients. The transpleural approach (right lateral intercostal) has been employed in 245 instances and the transabdominal approach (anterior) on 15 occasions. The patients' ages have ranged from 15 years to 82 years. There has been one death as a result of this technique (0.38 per cent). Five patients (1.9 per cent) have received intercostal block anesthesia for relief of pleural pain following the procedure.

Of the 250 patients in this series, 219 (88 per cent) had hepatomegaly and 81 patients (32 per cent) were icteric. Splenomegaly was present in 42 (17 per cent) and 24 patients (9.6 per cent) had demonstrable ascites. That the procedure has been used judiciously may be indicated by the diagnostic success in 83.3 per cent of the patients biopsied.

Table I indicates the pathological diagnoses encountered. Portal cirrhosis was the most frequent condition biopsied. In most instances the cirrhosis was evident clinically. In many patients the biopsy was helpful in following the progress of the disease. Fig. 1 pictures the Mallory bodies found in a patient with severe portal cirrhosis. A second biopsy five weeks later revealed no Mallory bodies present, consistent with the clinical improvement observed.

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The category of 'bile stasis' did not describe an exact diagnosis, but was in keeping with the clinical impression of many pathological conditions including common duct stone, hepatitis, metastatic malignancy in the liver, obstructing pancreatic carcinoma, papilloma of the bile duct, cholangitis, and even Hodgkins disease.

The diagnosis of 'normal' reported in 33 biopsies (13.2 per cent) in large part was the result of a vain search for hepatic pathology in unusual cases. These included the search for early cirrhosis, 'cardiac' cirrhosis in chronic congestive failure, malaria, hemochromatosis in diabetes mellitus, metastatic malignancy in the liver, and hepatic pathology secondary to acute cholecystitis.

TABLE I

NEEDLE BIOPSY OF THE LIVER

| Pathological Diagnoses | | No. Cases |
|---|---|---|
| Portal cirrhosis | | 113 (5)* |
| Mild | 45 | |
| Moderate | 45 | |
| Severe | 23 | |
| Normal | | 33 |
| Malignancy | | 28 |
| Metastatic carcinoma, hepatoma, lymphoma | | |
| Bile stasis | | 24 |
| Hepatitis | | 16 |
| Hemochromatosis | | 14 (4) |
| Fatty liver | | 9 |
| Specimen inadequate | | 8 |
| Biliary cirrhosis | | 4 |
| Sarcoid | | 3 |
| Chronic passive congestion | | 3 |
| Single diagnoses of: | | 5 (1) |
| Hemosiderosis, focal granulomata, miliary tuberculosis, glycogen storage disease, agnogenic myeloid metaplasia | | |
| | | 260 |

*Second biopsies, duplicate diagnoses.

The ten cases of hemochromatosis and one case of post-transfusion hemosiderosis are examples of the value of needle biopsy in comparison with other diagnostic techniques. It has made possible the early diagnosis of hemochromatosis in patients without diabetes mellitus or skin pigmentation.

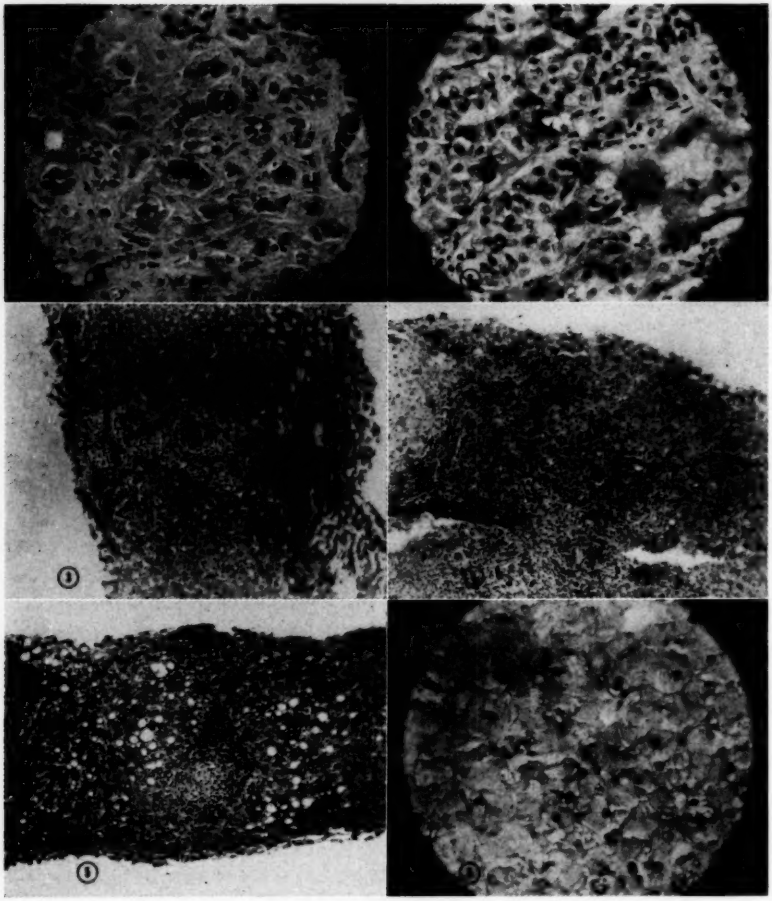

Fig. 1—Severe portal cirrhosis with Mallory bodies.

Fig. 2—Metastatic adenocarcinoma invading liver. Pleomorphic cells with large nucleii arranged in atypical acini. (Primary site in the stomach.)

Fig. 3—Acute cholangitis. The portal areas show infiltration of inflammatory cells.

Fig. 4—Acute hepatitis. Broad bands of inflammatory cells infiltrating liver and considerable destruction of liver tissue.

Fig. 5—Focal miliary granuloma with central necrosis and a whorled pattern of epithelioid cells. (Tuberculous etiology.)

Fig. 6—Excessive glycogen storage in diabetes mellitus. Extreme, diffuse vacuolization of liver cells.

Fig. 2 demonstrates metastatic adenocarcinoma in the liver of a 59 year-old-male. The primary site of malignancy was in the stomach. Needle biopsy technique obviated the necessity of laparotomy. Of the 35 patients in this series who were proven to have carcinoma in the liver, 22 or 63 per cent were demonstrated in the needle biopsy specimen. Five (55 per cent) of nine lymphoma's

were also demonstrated. Needle biopsy technique is indispensible in diagnosing this hepatic pathology. When malignancy has been found in the liver, subsequent laparotomy has been avoided unless extrahepatic obstructive jaundice is to be shunted. In no instance was a second biopsy attempt made when the initial biopsy failed to demonstrate malignancy. Ward, et. al.[2] have recommended a second biopsy attempt if the first fails to show the suspected neoplasm. In addition to the 35 patients with proven carcinoma of the liver, nine patients had negative needle biopsies and subsequent operative proof of no malignancy in the liver. Hence in 'looking for' metastatic carcinoma in the liver, correct information was derived by needle biopsy in 70 per cent. Eight specimens had bile stasis although malignant cells were not seen in the biopsy tissue. This evidence of obstructive jaundice was confirmatory of the diagnostic suspicion and was a significant aid in diagnosis.

Fig. 3 demonstrates acute cholangitis in a 50 year-old-male. Hepatomegaly, fever, and icterus led to suspicion of malignancy until the needle biopsy was done. Subsequent operation revealed a common duct calculus.

Fig. 4 demonstrates acute hepatitis in a 55 year-old-male. The destruction of liver tissue and the broad bands of inflammatory infiltration confirmed the diagnosis and defined the stage of the known liver disease.

Fig. 5 is an example of the needle biopsy revealing an unsuspected hepatic lesion. The 54 year-old-male had been observed with fever and hepatomegaly for 4 months. The diagnosis of metastatic malignancy was proved in error by needle biopsy. After demonstration of the focal miliary granuloma, tuberculosis was established as the etiology.

Fig. 6 presents excessive glycogen storage in a 19 year-old-male diabetic. Needle biopsy technique has proved an investigative tool for understanding the pathogenesis of clinical liver disease. The amount of liver glycogen in many cases of diabetes mellitus is now an interesting and unexplained finding.[1]

## *PRECAUTIONS*

Zamcheck and Klausenstock[3] in a review of 20,016 needle biopsies of the liver have found the procedure to be remarkably safe with a true mortality less than 1:1000. It is important that the procedure be performed by personnel who are not "misled by its apparent simplicity."[3] The patient must be cooperative in control of respiration. Certain absolute contraindications must be heeded, e.g. suppuration in areas of approach to the liver, obvious extrahepatic obstructive jaundice, manifest bleeding tendency, or impaired blood coagulation.

The single mortality in our series occurred in a 72 year-old-female with obstructive jaundice. Bile peritonitis had developed through a 1 cm. slit on the lateral right lobe of the liver.

## *CONCLUSIONS*

1. Needle biopsy of the liver in a series of 250 patients resulted in a correct diagnosis in 83.3 per cent.

2. Of these, the biopsy findings confirmed the clinical impression in 71 per cent, corrected an erroneous clinical diagnosis in 10 per cent, and revealed an unsuspected lesion in 2.3 per cent.

3. Biopsy findings were nonspecific and neither confirmed nor corrected the clinical diagnosis in 5.8 per cent.

4. The biopsy findings were misleading in the clinical diagnosis in 7.7 per cent.

5. An unsuccessful or inadequate specimen was obtained in 3.2 per cent.

6. Needle biopsy of the liver has proved an indispensable technique in the diagnosis of certain cases of liver disease.

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2. Ward, J., Schiff, L., Young, P., and Gall, E. A.: Needle biopsy of the liver. IX. Further experiences with malignant neoplasm, Gastroenterology 27:300, 1954.

3. Zamcheck, N., and Klausenstock, O.: Liver biopsy. II. The risk of needle biopsy, New England J. Med. 249:1062, 1953.

# DENTISTRY FOR THE HANDICAPPED CHILD

WILLIAM F. VIA, JR., D.D.S., M.S.*

Dental treatment for severely handicapped children has always been considered to be impossible. However, recent advances have simplified this problem to the extent that handicapped children can now receive expert dental care with very few exceptions. This has primarily been due to two basic developments: 1. New drugs and techniques have been developed to protect children with certain diseases during dental treatment; and, 2. The perfection of safer methods of general anesthesia, employing non-inflammable anesthetics. The purpose of this paper is not to describe the specific dental technics employed, but rather to present the general procedure followed.

Handicapped children may be roughly grouped into two general classifications:

First, those suffering from diseases that require medication or special dental techniques to preserve the health of the child during dental treatment. This group includes children with congenital heart disease, epilepsy, hemophilia, and rheumatic fever.

Secondly, those children that are mentally retarded, have cerebral palsy or have severe behavior problems which prevent them from cooperating sufficiently to undergo routine dental care. Examples of this group are those children suffering from congenital brain defects or irrepressible fear.

The first group, that is, those who cannot be treated by routine methods because of concomitant physical afflictions, are managed as follows:

A medical history of the patient is taken from the parent, including the reaction of the child to previous dental treatment. A preliminary visual examination of the mouth is done, and complete dental roentgenograms are obtained. Using the radiographs and the preliminary examination chart of the mouth, a complete appraisal of the patient's oral health is accomplished. The time required for treatment is estimated, and it is determined which teeth may be restored and which must be sacrificed.

Consultation is held with the patient's physician to determine the child's general condition and to decide what preoperative steps must be taken to adequately protect the health of the child before, during and after dental treatment. For those patients with congenital heart disease, rheumatic heart disease or with a history of rheumatic fever, the type and dosage of antibiotic medication, anesthesia and sedation is discussed. It is also decided whether the child may be treated as an out-patient or must be admitted to the hospital.

The type and amount of drugs to be given preoperatively to reinforce maintenance medication for children with a history of epileptiform seizures, mild cerebral palsy or mental retardation is also determined. The parent is then con-

*Associate, Division of Oral Surgery and Dentistry.

tacted, and the preoperative medication prescribed, the dental treatment program outlined, and appointments made for subsequent care.

If the patient is admitted to the hospital, the following plan is instituted:

Admission is arranged a day or two prior to operation to enable complete evaluation of the patient's condition and to aid the anesthesiologist in evaluating the risk of general anesthesia. Routine pre-anesthetic workup is done by a member of the pediatric staff. Consultation with a neurologist or pediatric cardiologist are obtained, if indicated. The anesthesiologist then determines whether the routine premedication for surgical general anesthesia, based upon the patient's weight and age, is adequate or should be supplemented with other drugs.

The patient is given the indicated premedication approximately one hour preoperatively and is moved to the operating room where the anesthesia is induced. The technique of anesthesia varies considerably depending upon the individual patient. However, it is usually necessary to insert an endotracheal tube via the mouth. After a surgical plane of anesthesia is reached and the tube is in position, a mouth prop is positioned and the posterior part of the mouth is packed with 4x8 gauze sponges. All fillings and extractions are completed for the patient at this time. Extreme care is used to prevent the aspiration of any debris or excess filling material.

After the completion of dental treatment, the oral cavity is searched for any extraneous particles that may have been previously missed. The mouth pack is removed, and the anesthesiologist terminates the anesthetic and removes the tube. The patient is moved to the recovery room where he remains until all reflexes become reactivated. Following complete recovery from anesthesia, he is returned to his room.

It is usually possible to discharge the patient on the day following the operation. Prior to discharge, the parent is instructed in adequate home care of the mouth, and dietary suggestions are made to reduce the occurrence of dental caries.

The child with a so-called behavior problem is handled in a somewhat different manner. The parent usually gives a history of having taken the child to various dentists only to have the child refuse treatment. Since this child usually has a mentality within the limits of normal, an attempt is made to allay his fear of dental treatment, for it is necessary to gain a child's confidence if dental treatment is to be possible on an out-patient basis.

If the parent is willing to cooperate, a series of orientation appointments are arranged for which no active treatment is planned. These appointments are used to establish rapport with the child and to prepare him for dental treatment in the future. If it is not possible to orient the child sufficiently to allow him to be cared for as an out-patient, he is admitted to the hospital, and the operation is done under general anesthesia as described previously. It is difficult to gain sufficient cooperation from most children for a smooth induction. It is, therefore, necessary to use the maximum allowable premedication, to minimize the psychological trauma of the trip to the operating room and induction of anesthesia.

When the treatment has been completed, home care of the mouth is discussed with the parent. Appointments are arranged for periodic dental examinations. It is hoped that, by seeing the patient for examination and oral prophylaxis at frequent intervals, it will be possible to allay his fears sufficiently so that future dental treatment may be accomplished in the usual manner.

## *SUMMARY*

Adequate dental treatment for severely handicapped children can only be performed safely in a hospital with the cooperation of various medical specialists and the facilities to care for any emergency.

The technique used at Henry Ford Hospital encompasses the following points:

1. An appraisal of the type and seriousness of the patient's handicap is made by consultations with specialists in appropriate Medical fields.

2. A dental treatment plan is formulated, including the necessary steps to protect the health of the child during the treatment.

3. The dental treatment is completed in the clinic or the operating room as the needs of the patient dictate.

4. The parent is instructed in the proper care of the patient's mouth at home, and follow-up appointments are arranged.

# DESCRIPTION OF NEW ORTHOPEDIC APPLIANCES

JOHN LYFORD, III, M.D.*

## "MATCHED" GENERAL UTILITY RETRACTORS FOR USE IN ORTHOPEDIC AND EXTREMITY SURGERY

It has been observed that for most orthopedic and extremity surgical procedures there were usually prepared in the sterile-instrument "set-up" eight to fourteen retractors of different designs and sizes. This armamentarium included the small skin "rakes" and "vein holders," progressing through the larger "appendix," "Hibbs," "army-navy," and "gall-bladder" retractors to the special patellar and tendon holders. This large number of instruments created confusion for the surgeon, assistants, and nurses.

To simplify this problem the following group of four "matched" general utility retractors was designed. During the four years that these retractors have been

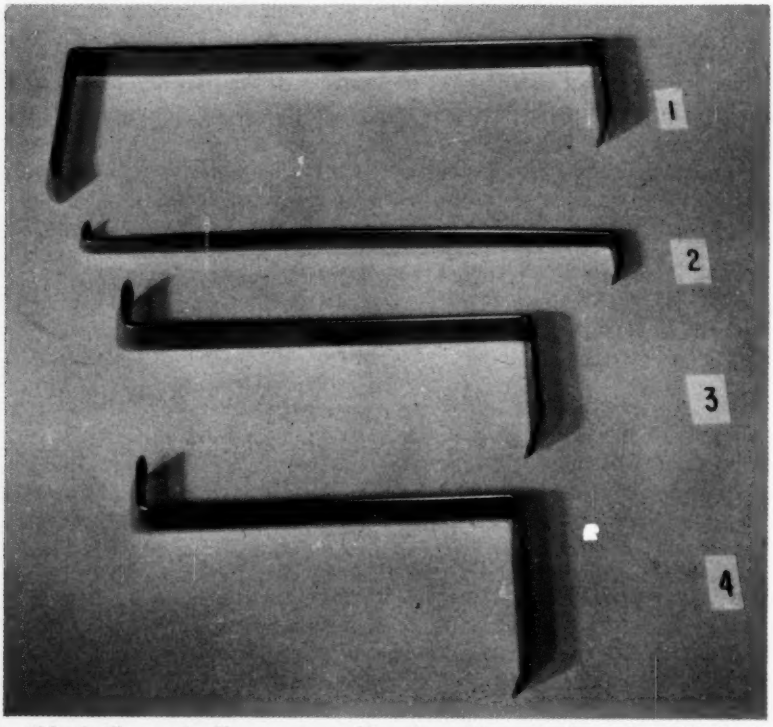


Fig. 1—"Matched" general utility retractors. Note the position and shape of the "holding" ends on each.

*Formerly Associate, Division of Orthopedic Surgery. At present, Chief, Department of Orthopedic Surgery, Veterans Administration Hospital, Louisville, Ky.

used they have met with acclaim by all who have employed them, and the number of retractors required to be prepared for orthopedic and extremity operative procedures has been reduced by approximately fifty per cent.

These retractors are illustrated in the accompanying photograph. All are made of stainless steel three-sixt enths of an inch thick, with those numbered 1, 3, and 4 in the photograph being five-eighths of an inch wide, and that numbered 2 being five-sixteenths of an inch wide. It is to be noted that the holding ends on all are curved-in slightly and bevelled to prevent slipping, but the edges are smooth to avoid tearing the soft tissues. Each retractor has holding ends of different lengths, doubling the function of each instrument. The length (or depth) of these ends are as follows: retractor number 1, two inches and three inches; number 2, three-eighths of an inch and three-fourths of an inch; number 3, one inch and two inches; number 4, one inch and three inches. The lengths of the retractors are thus: number 1, nine and one-fourth inches; number 2, nine inches; number 3, five and one-half inches; number 4, six and one-half inches. These dimensions were chosen as most satisfactory after trials of various combinations.

On the retractors with short ends—numbers 2, 3, and 4 in the photograph—the ends are turned in opposite directions to make for easier handling when in use. The retractor illustrated as number 2 has proved especially useful in procedures involving tendons and blood vessels in the hand, and that shown as number 1, in arthrotomies of the knee joint where the longer end serves very well for "supporting" the patella, and in spine-fusion operations.

## AN ADJUSTABLE DUAL-PURPOSE "OVERHEAD" READING TABLE FOR USE ON THE FOSTER-LYFORD REVERSIBLE ORTHOPEDIC BED

For the patient required to remain at complete horizontal bed rest, there are in use many accessories for aids in reading, such as "prism" eyeglasses for angle vision, and special overhead projection apparatus.

It had been observed that on occasion, for various reasons, such aids were not always available to the patient. Particularly there seemed to be an inconvenience in obtaining such accessories for those patients who were to be under treatment for relatively short periods, were to be at bed rest at home, or were to have intermittent rest periods in the supine position, such as individuals with spondylitis rhizomelic.

In this report there is described a "frame" with dual functions: it can be used as an "overhead" reading table, and it can serve as a "cradle" to prevent bed coverings from resting on the patient.

This "frame" has been designed for use primarily with the Foster-Lyford reversible orthopedic bed, but can be used readily on standard beds. The "frame" is constructed of light-weight metal tubing, is adjustable as to height and length, and can be disassembled into its component parts for easy storage in a drawer. The "table" on which the reading matter is supported is clear plastic. Plastic is

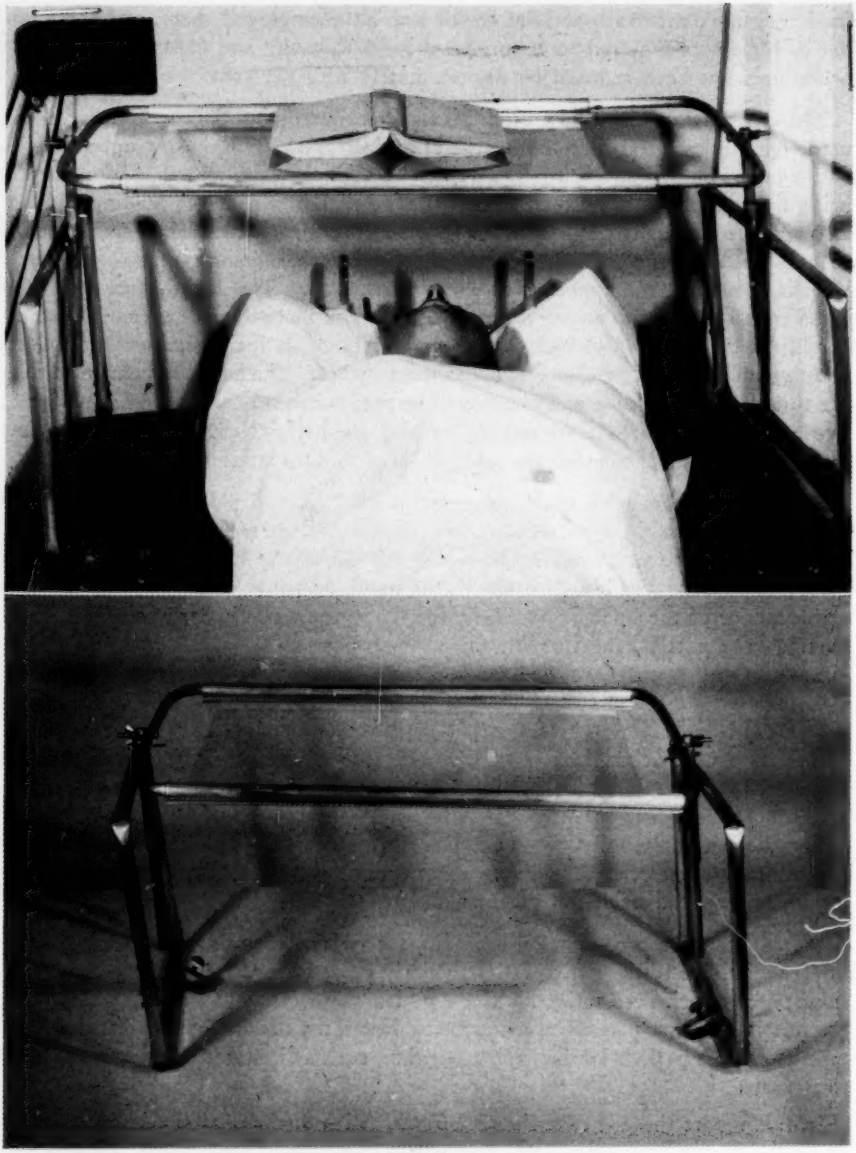

Fig. 1

used rather than glass to obviate injuries to the patient's face or eyes from breakage. With this apparatus the patient in the supine position can read easily books, magazines, or newspapers.

It is to be noted that for greatest comfort and facility by the patient in reading with the "overhead frame," the "table" supporting the reading matter should

be tilted cephalad about 15 degrees, and a source of illumination should be provided directed from below upwards.

In Figure 1 are illustrated the "overhead reading table," and an instance of its clinical use on the Foster-Lyford reversible orthopedic bed. Pages of the reading material are turned by the patient if his upper extremities are functioning, or by an attendant if the patient cannot use his arms and hands.

# FRIENDS OF THE INSTITUTE

OLIVER H. GAEBLER,* Ph.D., M.D.

In the closing paragraph of a tribute entitled: "Carl Von Voit, Master and Friend," Graham Lusk wrote: "Scientific progress does not depend on oratory, it does not depend on scribbling, it does not depend on men who sit at desks and think how to distribute funds; it depends on workers in the laboratory. A laboratory is like unto a city set on a high hill. Such a laboratory was that of Carl Voit."

This paragraph is entirely correct, and its ending is sublime. But there is a slightly sour phrase in it, indicating a fear which Lusk had that foundations would push the scientists around. Elsewhere in the cited article, and in his lectures, he repeatedly expressed his gratitude that research which he did in Voit's laboratory, though of no immediate value in connection with a government problem, was considered a service to the state, which paid for the supplies.

Every scientific publication begins with a title, the names of the authors, and the name of the institution or institutions where the work was done. Thus the topic of investigation, the persons who carried it out, and the role of organizations in providing facilities, cannot escape notice. Somewhere in footnotes there may be an acknowledgment to other persons, foundations, or associations whose financial support facilitated the work. Donors usually prefer it that way, and editors get insistent about it. Although the bulk of our support comes from institutions mentioned in the headings of papers, several grants from other sources have facilitated progress in the Biochemistry Department of this Institute to an extent that cannot be adequately acknowledged in footnotes.

The first of these grants was the Adelaide Skinner Fund, from which over $23,000 has been received to date. This money is being used in connection with our continuing studies of induced growth, and other problems related to cancer research. Another source of outside support, from which $27,431 has been received or assured at this writing, is the Michigan Chapter, Arthritis and Rheumatism Foundation. Local sponsors of this chapter mention with pride that it antedated the national foundation of which it is now a part. This grant has been extremely helpful in connection with studies of plasma protein patterns in rheumatoid arthritis and other diseases. Part of the money has also been used in connection with other problems in nitrogen metabolism in which the stable isotope, Nitrogen-15, is used. Most recently, we have received help from the American Heart Association. One of their Established Investigators has been appointed to fill a vacancy in this Department. These investigatorships make available average salary support of $7,000 per year for a period of five years. Our new staff member, Dr. Thomas P. Singer, is a well-known enzyme chemist, and will continue his investigations in this field. Additional support for this work, in the amount of $43,700 during

*Head, Department of Biochemistry, Edsel B. Ford Institute for Medical Research.

the next three years, has been approved by the National Heart Institute, U. S. Public Health Service.

Our thanks are due to the persons and organizations who have assisted our various projects with such substantial sums. Also, no gift to the Institute is too small to be both useful and appreciated. Mr. Edsel B. Ford, for whom the Institute is named, was a quiet progressive man, some of whose interests cannot be adequately memorialized by naming an expressway after him. A trip to the Art Institute reminds one of some of his other interests, and it is hoped that studies in the Edsel B. Ford Institute for Medical Research will commemorate still others.

# THE HENRY FORD HOSPITAL MEDICAL SOCIETY

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William L. Lowrie, M.D. ..... *Vice-President*
Robert J. Priest, M.D. ..... *Secretary*

## *Program for 1954-1955*

December 14, 1954—Tuesday, 8:15 p.m.—Henry Ford Hospital Auditorium

Primary Tumors of the Hand
Robert H. Clifford, M.D., *Surgeon in Charge, Division of Plastic Surgery*, Henry Ford Hospital
Gynecomastia
Richmond W. Smith, M.D., *Physician in Charge, Division of Endocrinology*, Henry Ford Hospital and Alexander P. Kelly, Jr., M.D., *Associate Surgeon, Division of Plastic Surgery*, Henry Ford Hospital

January 11, 1955—Tuesday, 8:15 p.m.—Henry Ford Hospital Auditorium

The Differential Diagnosis and Management of the Lymphomata
Charles A. Doan, M.D., *Dean and Director of Medical Research, Ohio State University*, Columbus, Ohio

February 8, 1955—Tuesday, 8:15 p.m.—Henry Ford Hospital Auditorium

Physiological and Clinical Aspects of Hypothermia
Robert D. Dripps, M.D., *Professor of Anesthesiology, University of Pennsylvania*, Philadelphia, Pennsylvania

March 8, 1955—Tuesday, 8:15 p.m.—Henry Ford Hospital Auditorium

Psychotherapy
Clarence B. Farrar, M.D., *Emeritus*
*Professor of Psychiatry, University of Toronto*, Canada

April 12, 1955—Tuesday, 8:15 p.m.—Henry Ford Hospital Auditorium

Surgical Management of Hypertension
Edgar A. Kahn, M.D., *Professor of Surgery, University of Michigan*, Ann Arbor, Michigan

May 10, 1955—Tuesday, 8:15 p.m.—Henry Ford Hospital Auditorium

The Roy D. McClure Memorial Lecture
The History of the Care and Repair of Wounds
Allen O. Whipple, M.D., *Emeritus*
*Professor of Surgery, College of Physicians and Surgeons*, New York, N. Y.

International Symposium

# CARDIOVASCULAR SURGERY

Recent Studies in Physiology, Diagnosis and Technics

March 17, 18, 19, 1955

The professional staff of the Henry Ford Hospital with the initial advice and support of The Board of Trustees and Dr. Robin C. Buerki, Executive Director, of the Henry Ford Hospital, is sponsoring an international symposium on the subject Cardiovascular Surgery, Recent Studies in Physiology, Diagnosis and Technics. This symposium will be held at the Henry Ford Hospital, March 17, 18, and 19, 1955, in the new auditorium. The preliminary program follows and has been prepared with the help of the advisory members.

Advisory Members:

| | |
|---|---|
| Richard J. Bing | Professor of Experimental Medicine, The Medical College of Alabama, Birmingham, Alabama |
| Michael E. Debakey | Professor of Surgery, Baylor University College of Medicine, Houston, Texas |
| Stanley Gibson | Consultant in Cardiology, Children's Memorial Hospital, Chicago, Illinois |
| Emile Holman | Professor of Surgery, Stanford University School of Medicine, San Francisco, California |

Local Members:

John W. Keyes, Secretary

D. Emerick Szilagyi

Conrad R. Lam, Chairman

Robert F. Ziegler

## *Tentative Program*

### First Morning Session

**Symposium on Diagnostic Technics**

Catheterization
Electrocardiography
Angiocardiography

**Panel on Diagnosis and Treatment of Pulmonary Stenosis**

Participants to discuss:
Late results of shunt operations
Direct operative procedures
Refinements in differential diagnosis

## First Afternoon Session

### Panel on Interatrial Septal Defect

Participants to discuss:

Recent advances in diagnosis
Closed operative technics
Open operative technics
Report on one-year follow-ups

### Interventricular Septal Defect

Diagnostic considerations
Technics of operations

### Evaluation of Operations for Transposition of the Great Vessels

### The Atypical Ductus Arteriosus

### Congenital Heart Disease in Infancy

## Second Morning Session

### Panel Discussion of Late Results of Mitral Commissurotomy

Participants will report on follow-up studies, with an attempt to evaluate "Radical" versus "conservative" operations.

### Refinements in the Technic of Operations for Mitral Stenosis. Operations for Mitral Regurgitation

## Second Afternoon Session

### Aortic Valvular Disease

Operations for Aortic Stenosis
Operations for Aortic Insufficiency

### Panel Discussion on Hypothermia in Cardiac Surgery

Participants will discuss:

Indications
Methods
Complications

## Review of the Present Status of the Subject of Cardiac Arrest

## Dinner Meeting

## Third Morning Session

## Review of the Present Status of Studies on the Etiology of Atherosclerosis.

## Surgery of Aneurysms

Thoracic

Abdominal

## Surgery of Occlusive Disease of Aorta and Peripheral Arteries

Thromboendarterectomy

Grafts

## Panel on Substitutes for Arterial Segments

Participants will discuss:

Homografts
Methods of sterilization and preservation

Plastic prostheses

Heterografts

(No afternoon session)

## Partial List of Participants from the United States and Canada

| | | | |
|---|---|---|---|
| Andrus, E. Cowles | Baltimore | Holman, Emile | San Francisco |
| Bahnson, Henry T. | Baltimore | Hufnagel, Charles A. | Washington |
| Bailey, Charles P. | Philadelphia | Keyes, John W. | Detroit |
| Bigelow, W. G. | Toronto | Kirklin, John W. | Rochester, Minn. |
| Bing, Richard C. | Birmingham | Lam, Conrad R. | Detroit |
| Blakemore, Arthur H. | New York | Likoff, William | Philadelphia |
| Creech, Oscar | Houston | Lillehei, C. Walton | Minneapolis |
| DeBakey, Michael | Houston | Muller, William H. | Los Angeles |
| Edwards, Jesse E. | Rochester, Minn. | Page, Irvine H. | Cleveland |
| Gerbode, Frank | San Francisco | Potts, Willis J. | Chicago |
| Gibson, Stanley | Chicago | Shumacker, Harris B., Jr. | Indianapolis |
| Glover, Robert | Philadelphia | Swan, Henry | Denver |
| Harken, Dwight E. | Boston | Szilagyi, D. Emerick | Detroit |
| Hellems, Harper | Detroit | Ziegler, Robert F. | Detroit |

The names of participants from other countries and additional participants from the United States will be found in the final program to be printed shortly.

# ABSTRACTS OF RECENT PUBLICATIONS OF THE PROFESSIONAL STAFF OF THE HENRY FORD HOSPITAL AND THE EDSEL B. FORD INSTITUTE FOR MEDICAL RESEARCH

## FOLLOW-UP 3 YEAR CLINICAL RESULTS OF COMBINED SUBTOTAL GASTRECTOMY AND SUBDIAPHRAGMATIC VAGOTOMY IN 108 CASES OF DUODENAL (AND JEJUNAL) ULCER. (COMPARISON ALSO OF RESULTS OBTAINED WITH GASTRODUODENAL AND GASTROJEJUNAL TYPES OF ANASTOMOSIS).

JAMES I. BALTZ, LAURENCE S. FALLIS, JOHN G. MATEER and JAMES BARRON. Gastroenterology 26:533, 1954.

The attempt to secure the best response to gastric surgery for peptic ulcer has resulted in progressive changes in operative procedures in recent years. Fallis and Barron have briefly reviewed the evolution of gastric surgery for this disease. Subtotal gastrectomy has been the single operation most commonly performed. This paper includes a partial review of the literature pertinent to surgery for peptic ulcer, an attempt to evaluate vagotomy, in combination with subtotal gastrectomy, in preventing the formation of anastomotic ulcer, and a preliminary report of the clinical results obtained in 128 patients having duodenal or jejunal ulcer upon whom a combination of subtotal gastrectomy and bilateral subdiaphragmatic vagotomy has been done, during a period from 1946 to mid-1951. The operative mortality has been 1.6%, representing 2 deaths. A total of 108 of these patients have had a satisfactory follow-up for an average of 38 months. An excellent result was obtained in 86.1% of these patients. A much longer period than 38 months of follow-up observation will be necessary to draw final conclusions as to the value and advisability of adding vagotomy to subtotal gastrectomy in an effort to prevent recurrent ulcer. In 68 of the above 108 patients a gastroduodenal anastomosis was established, and in the other 40 a gastrojejunal type of anastomosis was done. The total evidence at hand does not indicate, as yet, the superiority of either procedure, but we are continuing to do the gastroduodenostomy when the stomach can be properly mobilized and the anastomosis made without stress.

## *EFFECTS OF PROTEIN ANABOLIC HORMONES ON RATES OF PROTEIN DEGRADATION AND PROTEIN LOSS IN THE FASTING DOG.

PAUL D. BARTLETT and ANNE STEVENSON. Endocrinology 55:200, 1954.

Stimulation of the fasting adult female dog with growth hormone or testosterone propionate or a combination of growth hormone and testosterone propionate resulted in a reduction in the percentage of nitrogen of intravenously administered $N^{15}$ labeled glycine excreted in the total urinary nitrogen during the second, third, fourth, and fifth days of hormonal stimulation. The rate of protein degradation was not significantly reduced by either growth hormone or testosterone propionate. Stimulation of the same animals with growth hormone plus testosterone propionate, however, significantly reduced the rate of protein degradation. Reduction in

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the rate of protein loss, observed in all animals during stimulation with growth hormone or testosterone propionate or the combination of hormones was not significant.

*EFFECT OF DIHYDROCHOLESTEROL AND SOY BEAN STEROLS ON ELEVATED TISSUE CHOLESTEROL. W. T. Beher and W. L. Anthony. Proc. Soc. Exper. Biol. & Med. 86:589, 1954.

Dihydrocholesterol and soy bean sterols have attracted attention because they prevent accumulation of cholesterol in blood and tissues of animals receiving high cholesterol diets. While the exact mechanism of action remains undetermined, it appears that the principal effect of these substances is to diminish absorption of ingested cholesterol. It seemed important to determine whether mobilization of cholesterol already deposited in tissues can be influenced at all by adding soy bean sterols or dihydrocholesterol to the diet.

ACUTE FERROUS SULFATE POISONING; REPORT OF A NONFATAL CASE. Robert E. Birk and Sam K. Stallard. J. Pediat. 45:164, 1954.

A case of acute ferrous sulfate poisoning is presented in which a girl, 26 months old, ingested sixty-five iron capsules containing 13 gms. of ferrous sulfate. The child recovered; but in this dosage ferrous sulfate is a dangerous poison, as shown by 16 reported fatalities.

EXTRAMAMMARY PAGET'S DISEASE OF THE VULVA. Harold E. Bowman and Frank W. Hartman. Arch. Path. 58:304, 1954.

This paper reports the 17th case of extramammary Paget's disease of the vulva. This case is unusual in the respects that (a) the patient is alive and well 14 years following the diagnosis of this lesion and (b) the fact that the patient later developed an adenocarcinoma of the mammary gland. It is our hope that with the addition of more cases to the literature a trend or pattern may be established so that the true nature of this peculiar eczematoid picture with its characteristic cells may be better understood.

INTRA-ARTICULAR INJECTION OF HYDROCORTISONE INTO THE TEMPOROMANDIBULAR JOINT. Fred A. Henny. J. Oral Surg. 12:314, 1954.

Hydrocortisone has a specific action in the reduction of inflammatory changes within the temporomandibular joint. Its action is temporary; and if chronic irritative phenomena in the dental occlusion are allowed to persist, the pain is almost certain to recur. Roentgenographic evidence of erosion of the head of the condyloid process or proliferative changes within the joint are contraindications for injection of the drug. The treatment of such cases should be surgical; however, when indicated, intra-articular injection of hydrocortisone combined with correction of occlusal defects produces excellent results. The greatest benefit from the intraarticular injection of the drug is the reduction of inflammation, pain

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and trismus. Relief is obtained with relative rapidity, and it becomes possible to proceed with an orderly program of occlusal rehabilitation. The drug should not be considered as a specific cure but as a valuable adjunct in a well-organized program.

MULTIPLE MYELOMA SIMULATING APLASTIC ANEMIA. THOMAS N. JAMES and RAYMOND W. MONTO. Am. J. Med. 17:50, 1954.

Because general supportive care is usually the paramount initial concern in aplastic anemia, etiologic considerations are often deferred and even after study may remain enigmatic. The differential diagnosis seldom includes multiple myeloma. This report presents cases which were nosologically aplastic anemia but etiologically proved to be multiple myeloma. Multiple myeloma is extremely difficult to diagnose when it is presented as aplastic anemia. Although moderate anemia is one of the cardinal findings in multiple myeloma, severe anemia is an uncommon early manifestation. The pathogenesis of the anemia is not clearly understood. The three etiologic factors usually considered are as follows: (1) tumor replacement of normal marrow, (2) metabolic (toxic) inhibition of marrow function by products of myeloma cells and (3) renal failure with consequent azotemia.

CARDIAC RESUSCITATION FOLLOWING STANDSTILL, VENTRICULAR FIBRILLATION AND CORONARY AIR EMBOLISM. CONRAD R. LAM and THOMAS GEOGHEGAN. Am. Surgeon 20:928, 1954.

It is obvious that cessation of cardiac activity constitutes one of the gravest and most urgent situations for which remedial measures may be indicated. After 180 seconds of total failure of the circulation, there is great danger of irreversible changes in the brain. After 300 seconds, these changes are practically inevitable. The efficacy of intelligent treatment now is well established by the numerous reports of successful cardiac resuscitation. In order to achieve these results, the surgeon must have the best possible understanding of the mechanisms involved in the cessation of the circulation, and a definite plan of action must have been formulated before the emergency. Methods reviewed for cardiac stimulation include injected atropine, intra cardiac injection of adrenalin, heart massage, and potassium chloride and electric shock for defibrillation. The authors urge that measures be planned in advance.

TOXEMIA OF PREGNANCY—ACTH AND CORTISONE THERAPY. R. R. MARGULIS, C. PAUL HODGKINSON, W. C. RATTAN and J. S. JEWELL. Am. J. Obst. & Gynec. 67:1237, 1954.

Concepts regarding toxemia of pregnancy, the disease of theories, have been further complicated with the advent of ACTH and cortisone. Fragmentary evidence of the pharmacologic activity of these hormones in pregnancy has led to opposed theories of etiology and treatment of toxemia of pregnancy. Some have reasoned that the administration of cortisone would exert beneficial effects. Others have suggested that a disturbance in the adrenocortical steroid metabolism in pregnancy played an important role in the etiology of this disease. Practical

experience with the administration of ACTH and/or cortisone during pregnancy has not been sufficiently extensive for accurate evaluation. Twenty-four obstetrical patients received ACTH and/or cortisone during pregnancy. Nine patients suffering from toxemia of pregnancy received these hormones as part of their treatment. Fifteen patients received treatment during pregnancy for conditions not related to their pregnancy. ACTH and/or cortisone demonstrated no favorable influence upon toxemia. The administration of ACTH and/or cortisone did not produce symptoms of toxemia. These observations confirmed the impression that pregnant patients demonstrate an increased tolerance to ACTH and/or cortisone.

*AUTORADIOGRAPHIC STUDIES OF SURFACE DETAIL WITH CHROMIUM-51. L. E. Preuss. Nucleonics 12:30, 1954.

A unique approach combines methods of vacuum evaporation, shadow casting, and autoradiography. Details of metal surface structure are determined by a nondestructive technique to better than 40 microns in preliminary studies. Evidence for resolution of surface detail exceeding 40 $\mu$ has been demonstrated using $Cr^{51}$ with m.l.s. emulsion. It is conceivable that a resolution of about 5 $\mu$ may be achieved by using an isotope with emissions of other energy than the soft $\gamma$-rays associated with $Cr^{51}$. The gross apposition technique is simple and gives good topography for orientation. Disadvantages include resolution that is frequently poor because of bad contact, spurious abrasion exposures, and mechanical and thermal movement during exposure, which is magnified by techniques used for high magnification study.

REGIONAL HEARING LOSSES FROM INDUCED COCHLEAR INJURIES IN EXPERIMENTAL ANIMALS. Samuel Sutton and Harold F. Schuknecht. Ann. Otol., Rhinol. & Laryngol. 63:727, 1954.

Small cochlear lesions were created by mechanical injury with five needles or with controlled electrical current in the apical, middle, and basal turn of the cat cochlea. When the cortical test of auditory function was developed the opportunity was afforded of performing a test immediately after creating a lesion in the cochlea. Healthy young adult cats were used in this experiment. The function of one ear was destroyed by entering the auditory bulla and inserting a metal probe through the round window so as to completely macerate the cochlea. At this stage, the first of a series of cortical tests of auditory function was performed. The sound stimuli consisted of pure tones generated by an audio oscillator and keyed by an electronic switch at the rate of 1 per second. The tone pulses had a total duration of approximately 135 msecs and a rise time of 10 msecs. (For frequencies above 250 cycles, the output of the electronic switch was fed through a high pass filter to reduce keying transients.) The sound source was a permoflux PDR-10s earphone which was connected to the plastic coupler by a short length of flexible plastic tubing. The minimum stimulus intensity necessary to evoke a cortical response was determined for frequencies an octave or less apart, from 125 to 50,000 cycles. A selected region of the bony cochlear wall was thinned

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with a dental drill until the scala tympani and scala vestibuli could be visualized as light-absorbing regions with the spiral ligament as a white line between them. This thinning was continued until the remaining bone was only 20 to 30 micra in thickness. At this stage one of two procedures was followed. For some animals a fine needle was introduced through the thinned cochlear wall into the spiral ligament. For the others a spark or a heating effect produced by a radio-frequency current from an electrocautery unit was applied to the bone over the spiral ligament without entering the cochlear duct. Usually about 15 minutes elapsed from the moment of creating the cochlear lesion to the completion of the cortical test and another 30 minutes to the completion of intra-vital perfusion with Heidenhain-Susa solution.

CHEMICAL STERILIZATION OF ARTERIAL HOMOGRAFTS. PETER C. TRAFAS, RALPH E. CARLSON, GERALD A. LO GRIPPO and CONRAD R. LAM. Arch. Surg. 69:415, 1954.

The usefulness of homografts for bridging arterial defects has been demonstrated in laboratory animals and after operations in humans. In general, these grafts are functional after weeks or even months of storage if they have been removed aseptically and have been preserved in suitable solutions at low temperature. Naturally, there is no problem in obtaining adequate homograft material for animal experimentation, but it has been difficult to obtain sterile arterial segments from human cases. It would be advantageous if specimens removed at routine autopsies (and consequently unsterile) could be rendered sterile by a chemical process which would not denature the tissue in such a way as to compromise the results of grafting. Among the grafts treated with beta-propiolactone there was no instance of fatal hemorrhage and only one instance of thrombosis. Four of the 15 animals died in the early postoperative period of causes apparently not related to the grafts (extensive pnemonia in two, intussusception in one, no obvious cause in one). Ten of the survivors were killed after three months, and the other after almost two years. With the exception of a few tiny intimal ulcerations, the grafts appeared to be in excellent condition. Histologic study showed that the grafts did not differ significantly from the picture ordinarily seen when sterile, untreated grafts are implanted. Arterial homografts can be sterilized with the agent diacetylethylene, but there is an unacceptable incidence of early and late complications after implantation. The compound betapropiolactone effectively sterilizes the grafts and minimal adverse effects on the grafts have been apparent. Cautious clinical trial of this method of sterilization seems justified.

## MISUSED EXPRESSIONS

*To the Editor:*—From time to time in this section, a voice is raised in defense of correct medical phraseology. This appeal is not made by the purists in grammar, the classicists in language tradition, or the provincial perfectionists who are critical of all terminology except their own. It is made by those who have occasion to read manuscripts for publication and who review medical articles and books for the scientific literature. It is well, therefore, that at intervals attention should be called to the commoner errors in this field. Editors of scientific journals prob-

ably wince at some of the material they inspect, and it is well known that some papers presented for publication receive rejection slips because of the misuse of conventional expressions that are presumed to be in good favor. If a case report or a medical essay is worthy of being shared by others in the literature, it should be in acceptable scientific terminology.

Following are the most commonly misused expressions that occur even in "high places": "The physical examination *revealed*," "The roentgenogram *showed*," "The laboratory findings *demonstrated*," and combinations of these. Since inanimate subjects cannot have active verbs, these statements are grammatically and technically incorrect, but they have been absorbed into medical phraseology from one generation of medical students and authors to another. The acceptable manner of reproducing the above phrases is: "On physical examination there was (were)," "On roentgenograms there were," "The laboratory findings were." The correct usage is by far the simplest and easiest, without the blind acceptance of the hoary and repetitious.

Because the words serology, pathology, surgery, and chemistry are the names of specific medical sciences, it should be unnecessary to point out that the common clichés—"the *serology* was negative," "the *pathology* of the tissue was negative," "the patient was prepared for *surgery*," or "his *chemistry* was normal"—are all quite unacceptable. When these words are used in their adjective form, the statements have a definitive meaning, as: "The serological examination of the spinal fluid was within normal range," or "The patient was prepared for a surgical procedure (or operation)." The frequent statements "The patient was *placed* on penicillin" and "The infant was *put* on evaporated milk" are incorrect because, literally, these acts would be quite messy if really executed as stated. The terms administered, given, or fed would be acceptable in the correct expression of such phrases.

Many lesser violations of grammar and facile expression could be enumerated, and almost every earnest reader has many pet annoyances that he notes without possible redress. Among these are modifying adjectives to definite statement-words, such as "*rather* typical reaction," "*bluish* gray," or "*reddish* brown"; all these imply that the writer is not positive of his original meaning. Such expressions as "The patient had *no temperature*" and "The urine was *negative*" are obviously intolerable and are all too common misstatements that should not appear in good medical writing or speech. The standard and tried argument that common usage justifies the acceptance of these medical "hybrids" violates both technical ethnology and correct nomenclature. Their use in good medical writing often depreciates the industry and assiduous effort that the author has invested in his production.

—Reprinted from J. A. M. A. 156:274, 1954.

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# INDEX

## AUTHORS


Abraham, J. 155
Agey, W. L. *190
Alexander, E. J. * 11
Anthony, W. L. 99, 100, 154, 209
Appleman, R. M. 40

Baltz, J. I. 208
Barrett, J. L. 42
Barron, J. 33, *71, 153, 157, 208
Bartlett, P. D. 153, 208
Beher, W. T. 99, 100, 102, 154, 209
Behrmann, V. G. 154
Belknap, F. L., Jr. 37
Bellinger, D. H. * 56
Birk, R. E. 209
Bowman, H. E. 33, 155, 209
Blayney, J. R. 40
Bolstad, D. S. 101, *112
Brickman, G. L. 102
Brush, B. E. 33, *79, 101, 155, 157
Burger, J. H. * 28

Caldwell, J. R. * 7
Calder, J. R. 155
Carlson, R. 33, 212
Clifford, R. H. * 73
Coates, E. O., Jr. 102
Crigger, E. M. 102

Dicks, R. L. *140
Dickson, L. C., Jr. * 68
Dill, J. L. *112
Doub, H. P. 155
Drake, E. H. 35
Dumke, P. R. *176
Durham, R. H. 155
du Vigneaud, V. 187

Eyler, W. R. * 2

Fallis, L. S. 33, *71, 153, 208
Fischbein, J. W. *190
Fleming, J. L. 156
Forry, F. F. 33
Foulkes, R. H. 102

Gaebler, O. H. 99, 100, 102, 154, 202
Geoghegan, T. 35, 157, 210
Gish, J. R. 155
Goodman, E. D. 37
Goodrich, B. E. 37, 155
Gordon, E. J. 155
Grain, G. A. 104

Harrison, C. 161
Hartman, F. W. 34, 103, 154, 158, 159, 209
Head, E. S. 36
Hemmer, A. 105
Henny, F. A. 157, 209
Hodgkinson, C. P. 34, *44, 160, 210
Hoff, E. E. 162
Holliday, W. M. 99
Howard, P. J. *134
Howell, J. T. 35

James, T. N. 35, 103, 210
Jewell, J. S. 210
Johnson, E. A. 36
Johnston, J. A. 103

Kelly, A. R. 103, 152, 158, 159
Kemp, W. L. *106
Kenny, L. J. 36
Keyes, J. W. 35, 160
Kimura, R. S. 105
Knighton, R. S. *171
Knights, E. M., Jr. 103, 157

Lam, C. R. 36, 39, 157, 160, 210, 212
Leek, J. H. 40
Livingood, C. S. 36
LoGrippo, G. 103, 158, 212
Longabaugh, E. R. 42
Lowrie, W. L. * 79
Luzadre, J. H. 34, 160
Lyford, J., III *18, *86, *122, *198

McClure, R. F. 38
Marfey, S. P. 100
Margulis, R. R. 34, 160, 210
Marvel, H. R. 37, 162
Mateer, J. G. 208
Mathies, J. C. 37, 38, 160
Meade, G. M. 102
Mellinger, R. C. *13, 40, 162
Menagh, F. R. *130
Meyer, H. F. 212
Miller, J. M. *118
Monto, R. W. 35, 103, 155, 161, 210

Newman, E. V. *180
Nilasena, S. 36
Norris, E. R. 38

Ormond, J. K. *164

Patti, A. A. ..... 162
Pifer, P. W. ..... * 44
Pratt, J. P. ..... *125, 159
Preuss, L. E. ..... 38, 42, 104, 161, 211
Priest, R. J. ..... 39, *190
Proctor, L. D. ..... *171

Quinn, E. L. ..... 104, 162

Raftery, M. ..... 104
Rattan, W. C. ..... 210
Rebuck, J. W. ..... 39, 40, 103, 104, 105, 161, 162
Redfern, W. E. ..... * 79
Remp, D. G. ..... * 44
Ritchey, J. O. ..... 155
Rupe, C. E. ..... 159, 162
Ryan, R. J. ..... 162

Schimek, R. A. ..... * 89
Schuknecht, H. F. ..... 40, 41, 105, 211
Schumacher, E. E., Jr. ..... 104
Shaffer, J. H. ..... * 28
Shipley, R. E. ..... * 21
Sladen, F. J. ..... 42, *139
Smith, F. J. ..... 35
Smith, H. O. ..... 156
Smith, R. W., Jr. ..... *13, 162
Stallard, S. K. ..... 209
Steele, H. H. ..... *190
Steiner, L. J. ..... * 96
Stevenson, A. ..... 208
Sutton, S. ..... 211
Szilagyi, D. E. ..... 42, 105

Tazuma, J. J. ..... 159
Trafas, P. C. ..... 212

Via, W. F., Jr. ..... *195

Wahby, E. F. ..... 38
Watkins, T. W. ..... 103
Wright, K. C. ..... * 28

Yates, J. L. ..... 39, 105

Zeller, F., Jr. ..... 33, 101
Ziegler, R. F. ..... 43, 163

*Indicates the article appears in full in the BULLETIN*

## SUBJECTS

Abdomen. Acute conditions (Eyler) ..... * 2
  Exploration (Pratt) ..... *125
  Roentgenography (Eyler) ..... * 2
Abstracts ..... 33, 99, 152, 208
ACTH. In surgery (Brush) ..... 101
Adenoidectomy (Johnston & Watkins) ..... 103
Amyloidosis (Bolstad) ..... 101
Anemia. Aplastic (James & Monto) ..... 210
  Pernicious (Monto & Rebuck) ..... 161
Aneurysm. Aortic (Szilagyi & Hemmer) ..... 105
Ankle. Fracture (Fleming & Smith) ..... 156
Antimetabolites (Gaebler & others) ..... 99, 100
Aorta. Coarctation (Ziegler) ..... 163
Arteries. Transplantation (Trafas & others) ..... 212
Autoradiography (Preuss & Harrison) ..... 161
Barbital and barbital derivatives (Kelly) ..... 152
Benzoic acid (Gaebler & others) ..... 102
Blood. Fibrin (Hodgkinson & others) ..... 34, *44
    (Margulis & others) ..... 160
  Groups. (Rebuck) ..... 104
  Plasma. Sterilization (Hartman & others) ..... 103, 158
    (LoGrippo & others) ..... 158
    (Kelly & others) ..... 159
  Pressure. Intracardiac (Shipley) ..... * 21
Bone. Fibrous displasia (Caldwell) ..... * 7
Brain. Tumors (Knights) ..... 103, 157
Burns. Treatment (Lam) ..... 36
Capillaries. Permeability (Behrmann & Hartman) ..... 154

Carcinoma (Hartman) ..... 34
Cardiospasm (Lam) ..... 157
(Priest & Lam) ..... 39
Cardiovascular defects (Ziegler) ..... 163
Surgery. International Symposium ..... 205
Tentative Program ..... 205
Participants ..... 207
Chaplain. In hospital (Dicks) ..... *140
Cholesterol. Metabolism (Beher & others) ..... 154
(Beher & Anthony) ..... 99, 209
Cochlea *see* Ear. Internal
Colitis. Ulcerative (Fallis & Barron) ..... 33
Corti's organ *see* Ear. Internal
Cortisone. In surgery (Brush) ..... 101
Diabetes. Complications (Lowrie & others) ..... * 79
Dicks, Dr. Russell L. Introduction (Sladen) ..... *139
Disability (Steiner) ..... * 96
Ear. Emergencies (Schuknecht) ..... 40
Internal (Schuknecht) ..... 41
(Schuknecht & Kimura) ..... 105
(Sutton & Schuknecht) ..... 211
Edsel B. Ford Institute for Medical Research (Gaebler) ..... 202
Epilepsy (Proctor & Knighton) ..... *171
Esophagus. Pseudodiverticulum (Priest & Lam) ..... 39
Eyelids. Ptosis (Shimek) ..... * 89
Fistula. Suction tube for (Barron & Fallis) ..... * 71
Foot. Diabetic complications (Lowrie & others) ..... * 79
Paralysis (Lyford) ..... * 18
Gallbladder. Surgery (Brush & Zeller) ..... 101
Geriatrics (Sladen) ..... 42
Glutathione (Bartlett) ..... 153
Goiter. Nodular (Miller) ..... *118
Gold. Colloidal solutions (Preuss) ..... 104
Guillain-Barre syndrome (Raftery & others) ..... 104
Hand. Injuries (Clifford) ..... * 73
Hearing. Tests (Schuknecht) ..... 41
(Schuknecht & Kimura) ..... 105
(Sutton & Schuknecht) ..... 211
Heart. Auricular injury (James & Geoghegan) ..... 35
Catherization (Ziegler) ..... 43
Resusitated (Lam & Geoghegan) ..... 210
Henry Ford Hospital Medical Association ..... 147
Henry Ford Hospital Medical Society ..... 147, 204
Hernia. Diaphragmatic (Lam & Kenny) ..... 36
Hyperthyroidism (Mellinger & Smith) ..... * 13
Hyponatremic syndrome (Newman) ..... *180
Hypophyseal Growth Hormone, Nature and Actions. International Symposium 148
Program ..... 149
Participants ..... 151
Hypotension (Burger & others) ..... * 28
Immunohematology (Rebuck & Hoff) ..... 162
Inflammation. Effect of cortisone (Rebuck & Mellinger) ..... 40
International Congress on Thrombosis and Embolism ..... 155
Intersexuality (Pratt) ..... 159

Intestines. Anastomoses (Geoghegan & Brush) 157
Obstruction (McClure & Wahby) 38
Iron. Toxicity (Birk & Stallard) 209
Jaws. Cancer (Schuknecht & others) 40
Joints. Pathology (Lyford) * 86
Temporomandibular (Bellinger) * 56
(Henny) 209
Jugular Body. Tumors (Dill & Bolstad) *112
Knee. Pain (Lyford) *122
Liver. Disease (Priest & others) *190
Lungs. Cancer (Knights) 157, 103
Medicine. Practice (Kemp) *106
In India (Ormond) *164
Misused expressions in (Meyer) 212
Metals. Evaporation (Preuss) 38
Mitral valve. Duplication (Bowman & Forry) 33
Stricture. Recurrence (Keyes & Lam) 160
Mononucleosis. Infectious (Raftery & others) 104
Morphine (Dumke) *176
Mouth. Cancer (Schuknecht & others) 40
Myeloma. Multiple (Monto & Rebuck) 103
(James & Monto) 210
Myocardial infarction (Keyes & others) 35
Neoplasma. Transplantation (Foulkes) 102
Nose. Emergencies (Schuknecht) 40
Opium (Dumke) *176
Pancreatitis (Brush & others) 33
Peptic ulcer. Surgical therapy (Baltz & others) 208
Pepsin. Tuna (Norris & Mathies) 38
Periarteritis (Doub & others) 155
Phosphatase (Mathies) 160
(Mathies & Goodman) 37
Pituitary body. Hormones (de Vigneaud) 187
Plummer-Vinson syndrome (Howell & Monto) 35
Pneumonia. Bacterial (Marvel & others) 37
Pregnancy. Complications (Hodgkinson & others) 34
Toxemia (Margulis & others) 210
Protein. Metabolism (Bartlett & Stevenson) 208
Psychosomatic medicine (Dickson) * 68
Purpura. Hemorrhagica (Brush & others) 155
Retractor. For orthopedic surgery (Lyford) *198
Skin. Bacterial infections (Livingood & others) 36
Surface. Structure (Preuss) 211
Syphilis. Diagnosis. T.P.I. test (Menagh) *130
Table. Reading (Lyford) *199
Throat. Emergencies (Schuknecht) 40
Thrombophlebitis migrans (Durham) 155
Thyroid. Cancer (Miller) *118
Transplantation (Szilagyi & others) 42
Tongue. Cancer (Schuknecht & others) 40
Tonsillectomy (Johnston & Watkins) 103
Torulosis (Bowman & Ritchey) 155
Trauma. Surgical (Hodgkinson & others) * 44

Tube feeding (Barron & Fallis) ..... 153
(Henny & Barron) ..... 157
Tuberculin reaction. Skin test (Rebuck & Yates) ..... 39, 105
Tuberculosis. Pulmonary (Coates) ..... 101
Typhus fever (Rupe & others) ..... 162
Urine. Steroids (Smith & others) ..... 162
Vulva. Diseases (Bowman & Hartman) ..... 209
Words. Misuse of (Alexander) ..... * 11

**Indicates the article appears in full in the BULLETIN*